

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problems Mailbox.**

FIG.1A

	148	178	208	238	268	298
FRI-1	ALLVFLDIIIEWTTQETFPFKYLHYDPETGRQLLCDKCAPGTYLKQHC.TVRRKTLCV.PCPDY.SYTDSCD					
SW: TNR2_HUMAN	30	40	50	60	70	80
	HALPAQVAFTPYAPEGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCD					
	328					
FRI-1	YSYTDSWHTS					
	: : : :					
SW: TNR2_HUMAN	90	100	110	120	130	140
	STYTQLWNWVPECLSCGSRCSDDQVETQACTREQNRICTCRPGWCALSKQEGCRLCAPL					

FIG.1B

FRI-1	69	YLHYDPETGRQLLCDKCAPGTYLKQHC.TVRRKTLCV.PCPDY.SYTDSCD
TNFR profile	6	YHYDQNGRMCECHMCQPGHFLVKHCKQPKRDTVCHKPCPEPGVTYTDW
FRI-1	116	H
TNFR profile	56	H

Z Score = 8.29

FIG. 1C

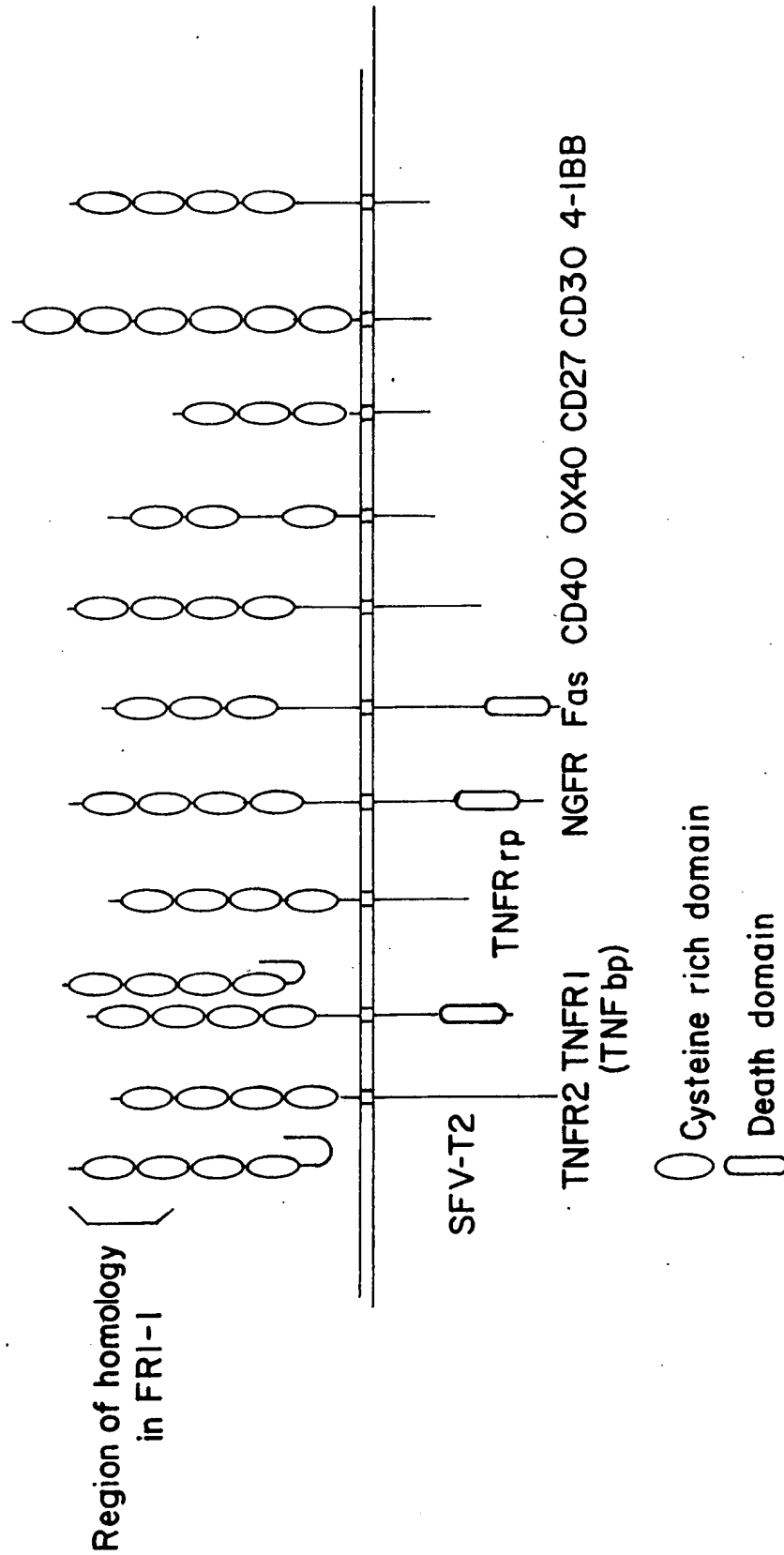


FIG.2A

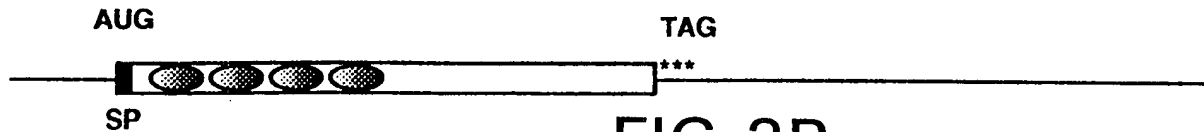


FIG.2B

10 30 50
ATCAAAGGCAGGGCATACTTCCTGTTGCCAGACCTTATATAAAACGTCATGTTTCGCCTG
70 90 110
GGCAGCAGAGAAGCACCTAGCACTGGCCCAGCGGCTGCCGCCTGAGGTTTCCAGAGGACC
130 150 170
ACAATGAACAAGTGGCTGTGCTGTGCACTCCTGGTGTCTTGGACATCATTGAATGGACA
M N K W L C C A L L V F L D I I E W T
190 210 230
ACCCAGGAAACCTTTCCTCCAAAATACTTGCATTATGACCCAGAAACCGGACGTCAGCTC
T Q E T F P P K Y L H Y D P E T G R Q L
250 270 290
TTGTGTGACAAATGTGCTCCTGGCACCTACCTAAACAGCACTGCACAGTCAGGAGGAAG
L C D K C A P G T Y L K Q H C T V R R K
310 330 350
ACACTGTGTGTCCCTTGCCCTGACTACTCTTATACAGACAGCTGGCACACGAGTGATGAA
T L C V P C P D Y S Y T D S W H T S D E
370 390 410
TGCGTGTACTGCAGCCCCGTGTGCAAGGAAGTGCAGACCGTGAAACAGGAGTGCAACCGC
C V Y C S P V C K E L Q T V K Q E C N R
430 450 470
ACCCACAACCGAGTGTGCGAATGTGAGGAAGGGCGCTACCTGGAGCTCGAATTCTGCTTG
T H N R V C E C E E G R Y L E L E F C L
490 510 530
AAGCACCGGAGCTGTCCCCCAGGCTTGGGTGTGCTGCAGGCTGGGACCCAGAGCGAAAC
K H R S C P P G L G V L Q A G T P E R N
550 570 590
ACGGTTTGCAAAAGATGTCCGGATGGGTTCTTCTCAGGTGAGACGTCATCGAAAGCACCC
T V C K R C P D G F F S G E T S S K A P
610 630 650
TGTAGGAAACACACCAACTGCAGCTCACTTGGCCTCCTGCTAATTGAGAAAGGAAATGCA
C R K H T N C S S L G L L L I Q K G N A
670 690 710
ACACATGACAATGTATGTTCCGGAAACAGAGAAGCAACTCAAATTTGTGGAATAGATGTC
T H D N V C S G N R E A T Q N C G I D V
730 750 770
ACCCTGTGCGAAGAGGCATTCTTCAGGTTTGTGCTGTGCCTACCAAGATTATACCGAATTGG
T L C E E A F F R F A V P T K I I P N W
790 810 830
CTGAGTGTTCTGGTGGACAGTTTGCCTGGGACCAAAGTGAATGCAGAGAGTGTAGAGAGG
L S V L V D S L P G T K V N A E S V E R
850 870 890
ATAAAACGGAGACACAGCTCGCAAGAGCAAACCTTTCCAGCTACTTAAGCTGTGGAAGCAT
I K R R H S S Q E Q T F Q L L K L W K H
910 930 950
CAAAACAGAGACCAGGAAATGGTGAAGAAGATCATCCAAGACATTGACCTCTGTGAAAGC
Q N R D Q E M V K K I I Q D I D L C E S
970 990 1010
AGTGTGCAACGGCATATCGGCCACGCGAACCTCACCACAGAGCAGCTCCGCATCTTGATG
S V Q R H I G H A N L T T E Q L R I L M

FIG. 2C

```

1030      1050      1070
GAGAGCTTGCCTGGGAAGAAGATCAGCCCAGACGAGATTGAGAGAACGAGAAAGACCTGC
E S L P G K K I S P D E I E R T R K T C
1090      1110      1130
AAACCCAGCGAGCAGCTCCTGAAGCTACTGAGCTTGTGGAGGATCAAAAATGGAGACCAA
K P S E Q L L K L L S L W R I K N G D Q
1150      1170      1190
GACACCTTGAAGGGCCTGATGTACGCACTCAAGCACTTGAAAGCATACCACTTTCCCAAA
D T L K G L M Y A L K H L K A Y H F P K
1210      1230      1250
ACCGTCACCCACAGTCTGAGGAAGACCATCAGGTTCTTGACAGCTTCACCATGTACCGA
T V T H S L R K T I R F L H S F T M Y R
1270      1290      1310
TTGTATCAGAAACTCTTTCTAGAAATGATAGGGAATCAGGTTCAATCAGTGAAGATAAGC
L Y Q K L F L E M I G N Q V Q S V K I S
1330      1350      1370
TGCTTATAGTTAGGAATGGTCACTGGGCTGTTTCTTCAGGATGGGCCAACACTGATGGAG
C L
1390      1410      1430
CAGATGGCTGCTTCTCCGGCTCTTGAAATGGCAGTTGATTCCTTTCTCATCAGTTGGTGG
1450      1470      1490
GAATGAAGATCCTCCAGCCCAACACACACACTGGGGAGTCTGAGTCAGGAGAGTGAGGCA
1510      1530      1550
GGCTATTTGATAATTGTGCAAAGCTGCCAGGTGTACACCTAGAAAGTCAAGCACCCCTGAG
1570      1590      1610
AAAGAGGATATTTTTATAACCTCAAACATAGGCCCTTTCCTTCCTCTCCTTATGGATGAG
1630      1650      1670
TACTCAGAAGGCTTCTACTATCTTCTGTGTCATCCCTAGATGAAGGCCTCTTTTATTTAT
1690      1710      1730
TTTTTTTATTCTTTTTTTTCGGAGCTGGGGACCGAACCCAGGGCCTTGCGCTTGCGAGGCAA
1750      1770      1790
GTGCTCTACCACTGAGCTAAATCTCCAACCCCTGAAGGCCTCTTTCTTTCTGCCTCTGAT
1810      1830      1850
AGTCTATGACATTCTTTTTTCTACAATTTCGTATCAGGTGCACGAGCCTTATCCCATTGTG
1870      1890      1910
AGGTTTCTAGGCAAGTTGACCGTTAGCTATTTTTCCCTCTGAAGATTGATTTCGAGTTGC
1930      1950      1970
AGACTTGGCTAGACAAGCAGGGGTAGGTTATGGTAGTTTATTTAACAGACTGCCACCAGG
1990      2010      2030
AGTCCAGTGTTTCTTGTTCCCTCTGTAGTTGTACCTAAGCTGACTCCAAGTACATTTAGTA
2050      2070      2090
TGAAAAATAATCAACAAATTTTATTTCCTTCTATCAACATTGGCTAGCTTTGTTTCAGGGC
2110      2130      2150
ACTAAAAGAACTACTATATGGAGAAAGAATTGATATTGCCCCCAACGTTCAACAACCCA
2170      2190      2210
ATAGTTTATCCAGCTGTCATGCCTGGTTCAGTGTCTACTGACTATGCGCCCTCTTATTAC
2230      2250      2270
TGCATGCAGTAATTCAACTGGAAATAGTAATAATAATAATAGAAATAAAATCTAGACTCC
2290      2310      2330
ATTGGATCTCTCTGAATATGGGAATATCTAACTTAAGAAGCTTTGAGATTTTCAGTTGTGT
2350      2370      2390
TAAAGGCTTTTATTAAAAAGCTGATGCTCTTCTGTAAAAGTTACTAATATATCTGTAAGA
2410      2430
CTATTACAGTATTGCTATTTATATCCATCCAG
```

FIG. 2D

[illegible]

WZ. 61

[illegible][illegible][illegible]

FIG. 3A

Basic
 Acidic
 β Form
 β Break

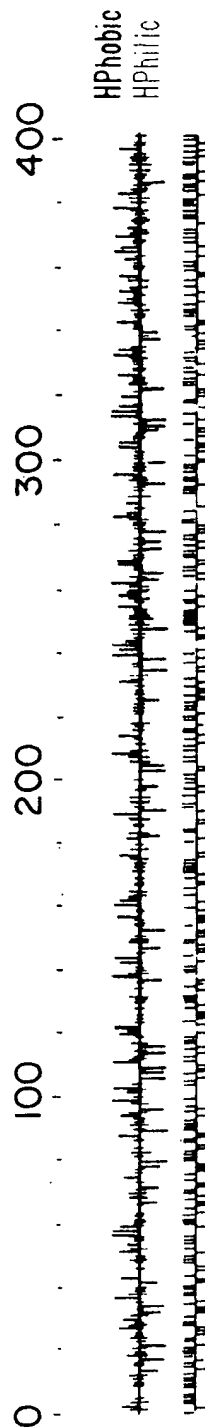


FIG. 3B

Chou &
 Fosman

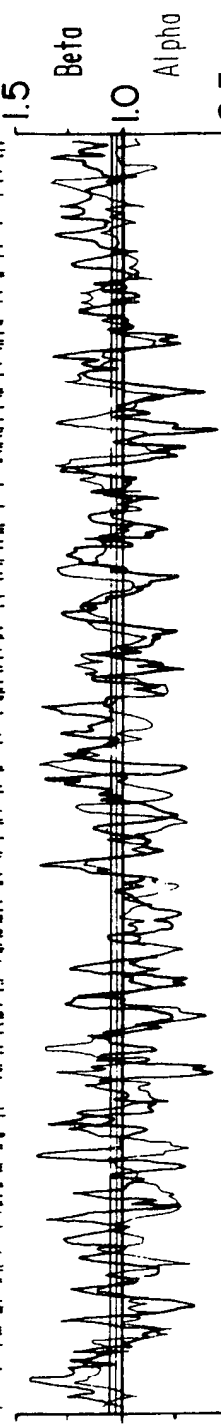


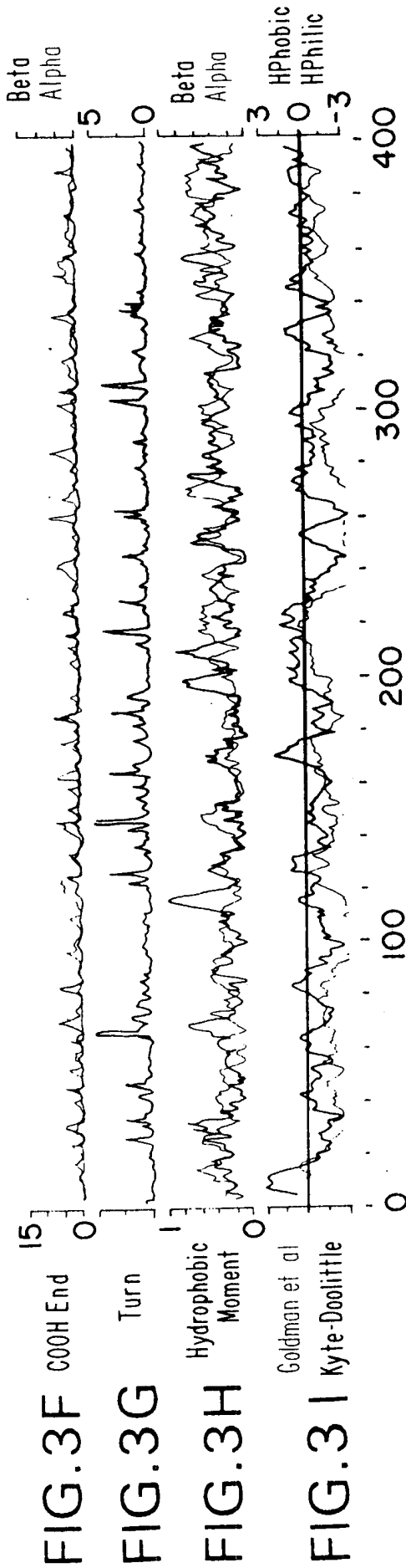
FIG. 3C

α Form
 α Break
 NH₂ End



FIG. 3D





TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.4A

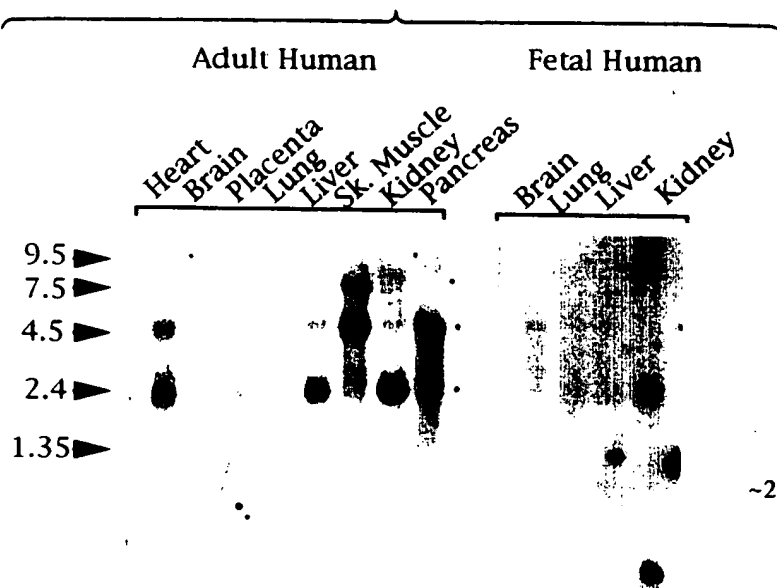
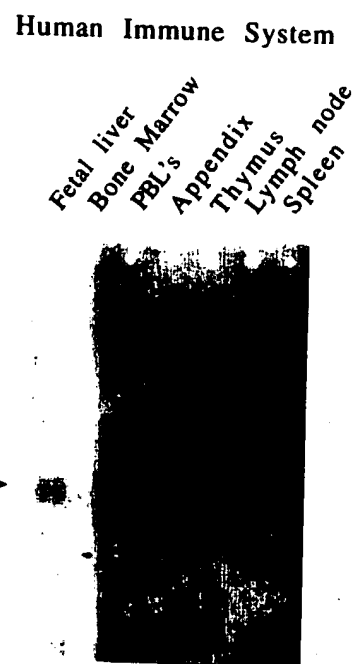
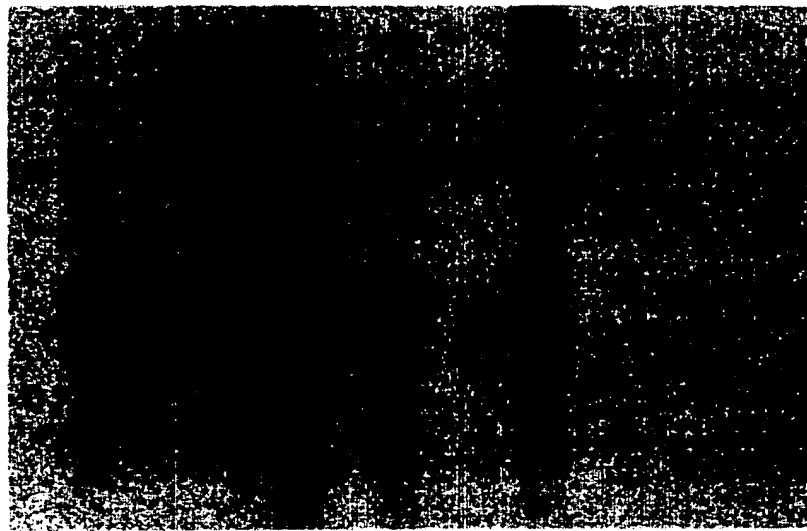


FIG.4B



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.5



2 11 16 17 22 28 33 38 45 Kb 1 12 18 30
Transgenic Founders Controls

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.6A

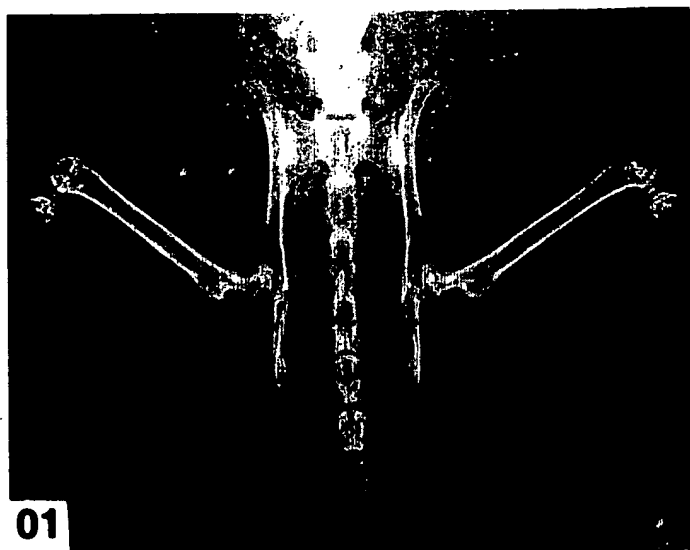


FIG.6B

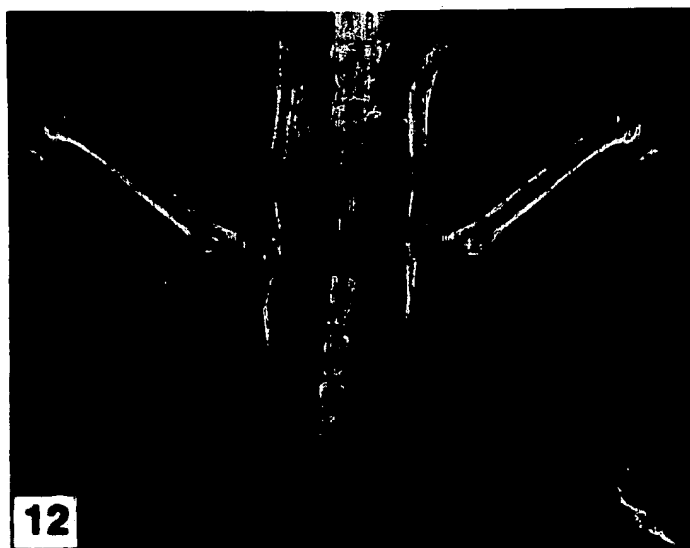


FIG.6C



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.6D

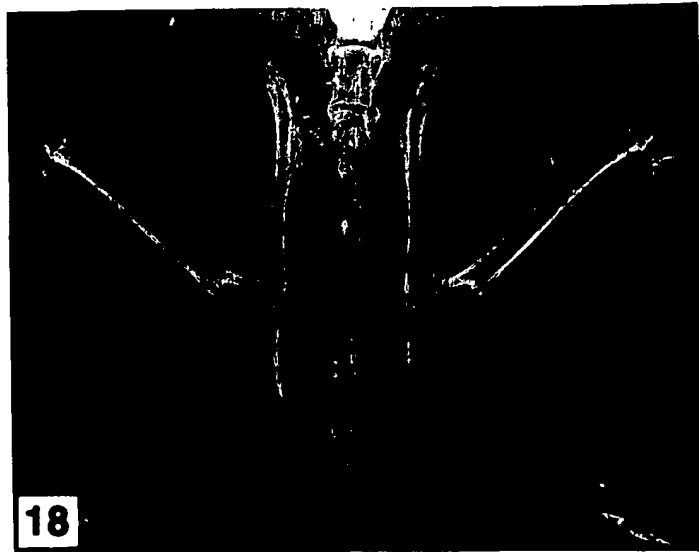


FIG.6E

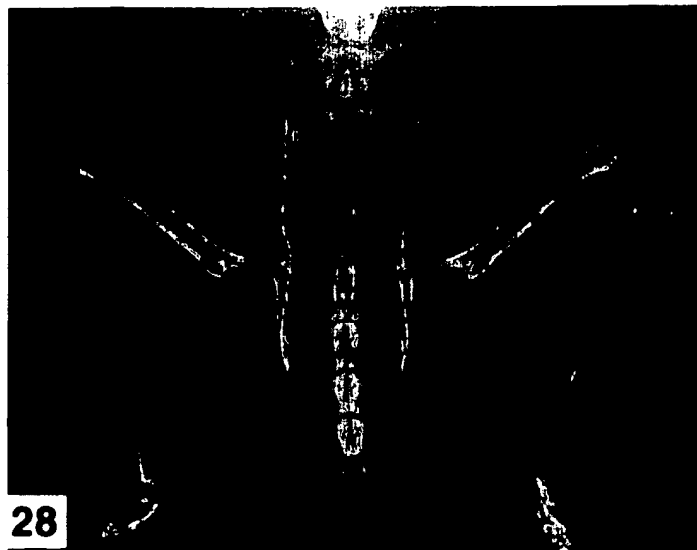
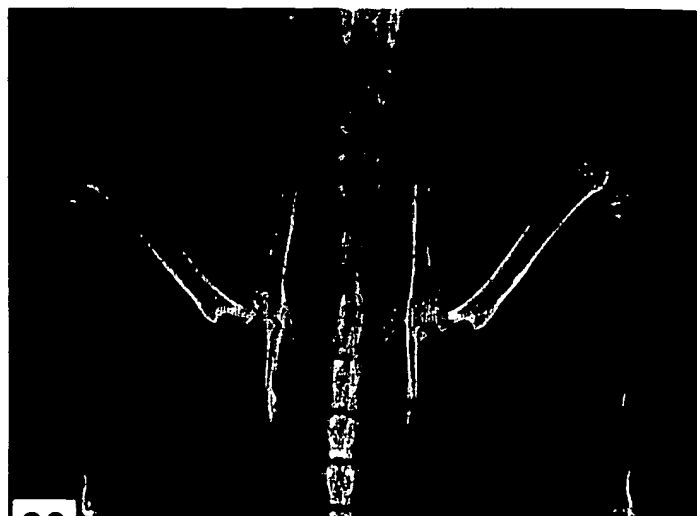


FIG.6F



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.6G

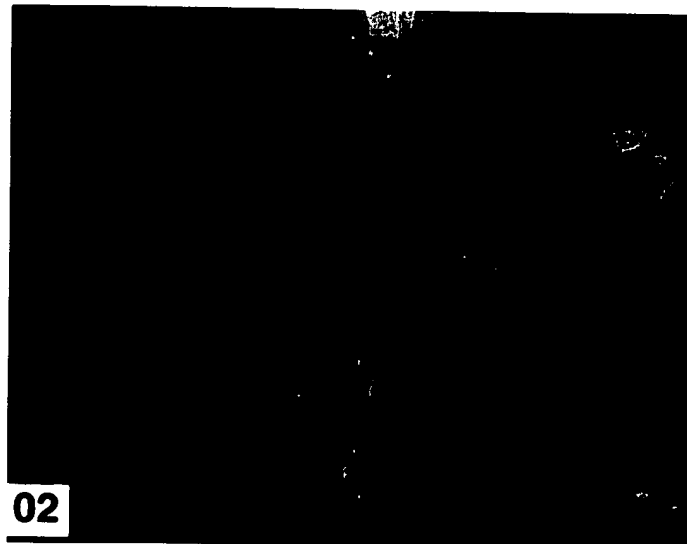
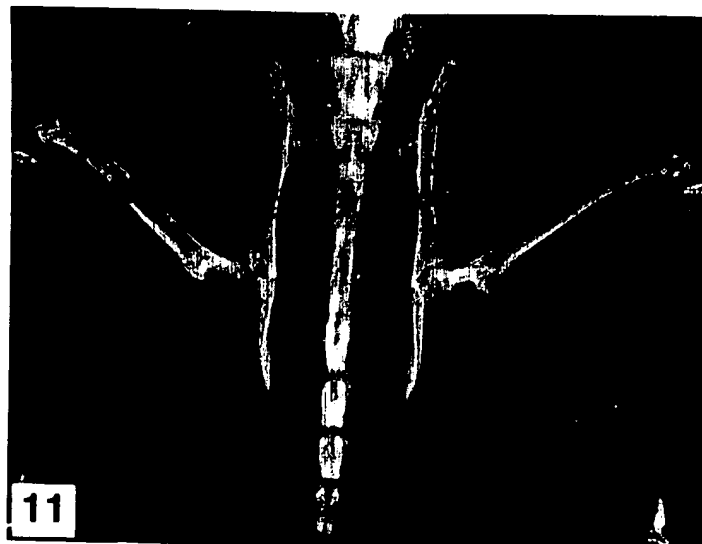


FIG.6H

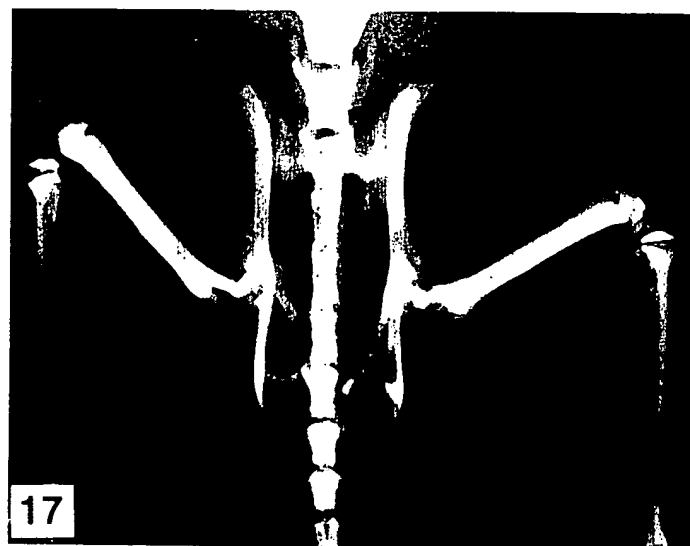


TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.6I



FIG.6J



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.7A

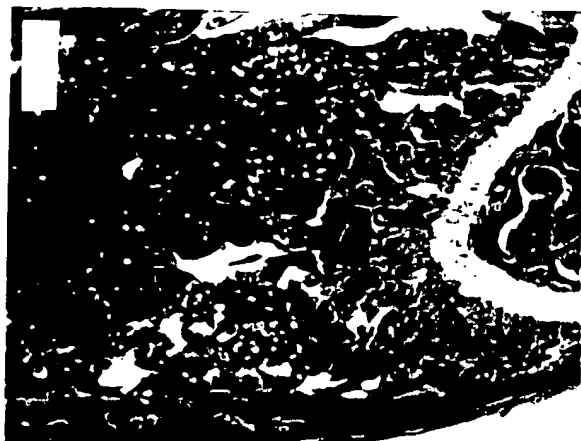


FIG.7B



FIG.7C



FIG.7D



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.7E



FIG.7F

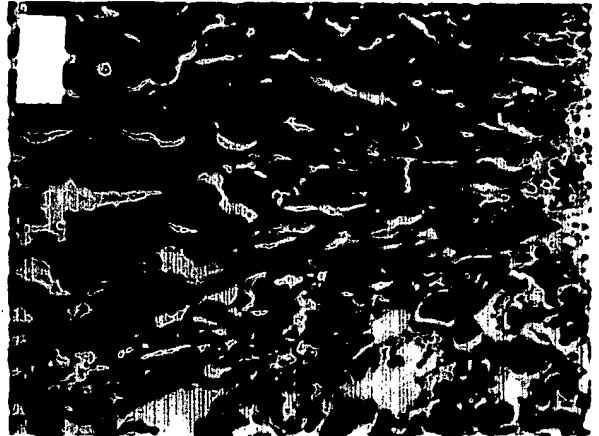
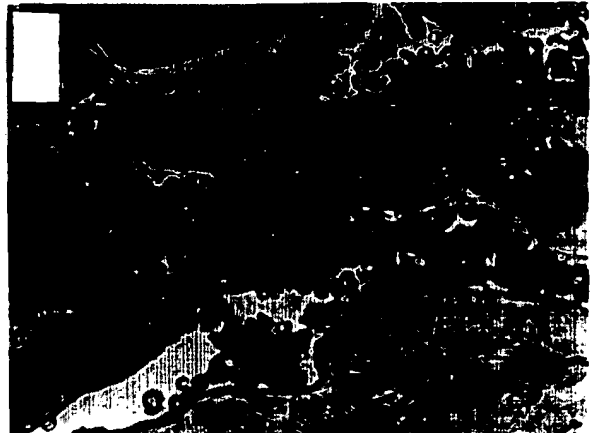


FIG.7G



FIG.7H



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.8A



FIG.8B



FIG.8C

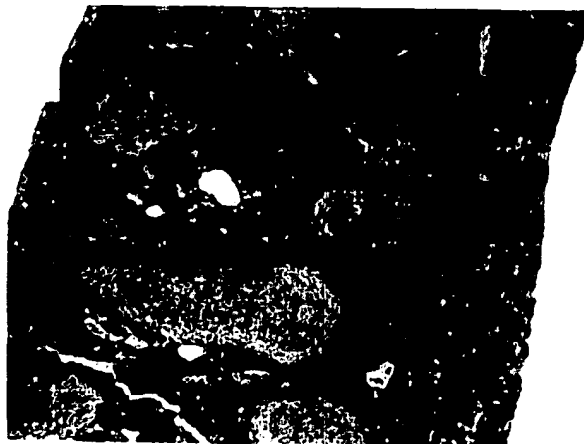


FIG.8D



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.9A

```

      10              30              50
CCTTATATAARACGTCATGATTGCCTGGGCTGCAGAGACGCACCTAGCACTGACCCAGCG
      70              90              110
GCTGCCTCCTGAGGTTTCCCGAGGACCACAATGAACAAGTGGCTGTGCTGCGCACTCCTG
      130              150              170
      M N K W L C C A L L
GTGCTCCTGGACATCATTTGAATGGACAACCCAGGAAACCCTTCCTCCAAAGTACTTGCAT
      190              210              230
V L L D I I E W T T O E T L P P K Y L H
TATGACCCAGAACTGGTCATCAGCTCCTGTGTGACAAATGTGCTCCTGGCACCTACCTA
      250              270              290
Y D P E T G H Q L L C D K C A P G T Y L
AAACAGCACTGCACAGTGAGGAGGAAGACATTGTGTGTCCCTTGCCCTGACCACTCTTAT
      310              330              350
K Q H C T V R R K T L C V P C P D H S Y
ACGGACAGCTGGCACACCAGTGATGAGTGTGTGTATTGCAGCCCAGTGTGCAAGGAACTG
      370              390              410
T D S W H T S D E C V Y C S P V C K E L
CAGTCCGTGAAGCAGGAGTGCAACCGCACCCACAACCGAGTGTGTGAGTGTGAGGAAGGG
      430              450              470
Q S V K Q E C N R T H N R V C E C E E G
CGTTACCTGGAGATCGAATTCTGCTTGAAGCACCGGAGCTGTCCCCGGGCTCCGGCGTG
      490              510              530
R Y L E I E F C L K H R S C P P G S G V
GTGCAAGCTGGAACCCCAGAGCGAAACACAGTTTGCAAAAAATGTCCAGATGGGTTCTTC
      550              570              590
V Q A G T P E R N T V C K K C P D G F F
TCAGGTGAGACTTCATCGAAAGCACCCCTGTATAAAACACACGAACTGCAGCACATTTGGC
      610              630              650
S G E T S S K A P C I K H T N C S T F G
CTCCTGCTAATTCAGAAAGGAAATGCAACACATGACAACGTGTGTTCCGGAAACAGAGAA
      670              690              710
L L L I Q K G N A T H D N V C S G N R E
GCCACGCAAAAAGTGTGGAATAGATGTCAACCCTGTGTGAAGAGGCCTTCTTCAGGTTTGCT
      730              750              770
A T Q K C G I D V T L C E E A F F R F A
GTTCTACCAAGATTATACCAAATTGGCTGAGTGTTTTGGTGGACAGTTTGCCTGGGACC
V P T K I I P N W L S V L V D S L P G T

```

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.9B

```

      790              810              830
AAAGTGAATGCCGAGAGTGTAGAGAGGATAAAACGGAGACACAGCTCACAAAGAGCAAACC
K  V  N  A  E  S  V  E  R  I  K  R  R  H  S  S  Q  E  Q  T
      850              870              890
TTCCAGCTGCTGAAGCTGTGGAAACATCAAACAGAGACCAGGAAATGGTGAAGAAGATC
F  Q  L  L  K  L  W  K  H  Q  N  R  D  Q  E  M  V  K  K  I
      910              930              950
ATCCAAGACATTGACCTCTGTGAAAGCAGCGTGCAGCGGCATCTCGGCCACTCGAACCTC
I  Q  D  I  D  L  C  E  S  S  V  Q  R  H  L  G  H  S  N  L
      970              990              1010
ACCACAGAGCAGCTTCTTGCCTTGATGGAGAGCCTGCCTGGGAAGAAGATCAGCCCAGAA
T  T  E  Q  L  L  A  L  M  E  S  L  P  G  K  K  I  S  P  E
      1030             1050             1070
GAGATTGAGAGAACGAGAAAGACCTGCAAATCGAGCGAGCAGCTCCTGAAGCTACTCAGT
E  I  E  R  T  R  K  T  C  K  S  S  E  Q  L  L  K  L  L  S
      1090             1110             1130
TTATGGAGGATCAAAAATGGTGACCAAGACACCTTGAAGGGCCTGATGTATGCCCTCAAG
L  W  R  I  K  N  G  D  Q  D  T  L  K  G  L  M  Y  A  L  K
      1150             1170             1190
CACTTGAAAAACATCCCACCTTTCCCAAAACTGTCACCCACAGTCTGAGGAAGACCATGAGG
H  L  K  T  S  H  F  P  K  T  V  T  H  S  L  R  K  T  M  R
      1210             1230             1250
TTCCTGCACAGCTTCACAATGTACAGACTGTATCAGAAGCTCTTTTGTAGAAATGATAGGG
F  L  H  S  F  T  M  Y  R  L  Y  Q  K  L  F  L  E  M  I  G
      1270             1290             1310
AATCAGGTTCAATCCGTGAAAATAAGCTGCTTATAACTAGGAATGGTCACTGGGCTGTTT
N  Q  V  Q  S  V  K  I  S  C  L

CTTCA
```

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.9C

```

      10      30      50
GTATATATAACGTGATGAGCGTACGGGTGCGGAGACGCACCGGAGCGCTCGCCCAGCCGC
      70      90     110
CGYCTCCAAGCCCCTGAGGTTTCCGGGGACCACAATGAACAAGTTGCTGTGCTGCGCGCT
                                M N K L L C C A L
      130     150     170
CGTGT'TTCTGGACATCTCCATTAAGTGGACCACCCAGGAAACGTTTCCTCCAAAGTACCT
V F L D I S I K W T T Q E T F P P K Y L
      190     210     230
TCATTATGACGAAGAAACCTCTCATCAGCTGTTGTGTGACAAATGTCCTCCTGGTACCTA
H Y D E E T S H Q L L C D K C P P G T Y
      250     270     290
CCTAAAACAACACTGTACAGCAAAGTGGAAGACCGTGTGCGCCCCCTTGCCCTGACCACTA
L K Q H C T A K W K T V C A P C P D H Y
      310     330     350
CTACACAGACAGCTGGCACACCAGTGACGAGTGTCTATACTGCAGCCCCGTTGTGCAAGGA
Y T D S W H T S D E C L Y C S P V C K E
      370     390     410
GCTGCAGTACGTCAAGCAGGAGTGCAATCGCACCCACAACCGCGTGTGCGAATGCAAGGA
L Q Y V K Q E C N R T H N R V C E C K E
      430     450     470
AGGGCGCTACCTTGAGATAGAGTTCTGCTTGAAACATAGGAGCTGCCCTCCTGGATTTGG
G R Y L E I E F C L K H R S C P P G F G
      490     510     530
AGTGGTGCAAGCTGGAACCCCAAGCGAAATACAGTTTGCAAAAGATGTCCAGATGGGTT
V V Q A G T P E R N T V C K R C P D G F
      550     570     590
CTTCTCAAATGAGACGTCATCTAAAGCACCCCTGTAGAAAACACACAAATTGCAGTGTCTT
F S N E T S S K A P C R K H T N C S V F
      610     630     650
TGGTCTCCTGCTAACTCAGAAAGGAAATGCAACACACGACAACATATGTTCCGGAAACAG
G L L L T Q K G N A T H D N I C S G N S
      670     690     710
TGAATCAACTCAAAAATGTGGAATAGATGTTACCCTGTGTGAGGAGGCATTCTTCAGGTT
E S T Q K C G I D V T L C E E A F F R F
      730     750     770
TGCTGTTCTACAAAGTTTACGCCTAACTGGCTTAGTGTCTTGGTAGACAATTTGCCTGG
A V P T K F T P N W L S V L V D N L P G

```

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.9D

```

      790              810              830
CACCAAAGTAAACGCAGAGAGTGTAGAGAGGATAAAACGGCAACACAGCTCACAAGAACA
  T  K  V  N  A  E  S  V  E  R  I  K  R  Q  H  S  S  Q  E  Q
      850              870              890
GACTTTCAGCTGCTGAAGTTATGGAAACATCAAAACAAAGACCAAGATATAGTCAAGAA
  T  F  Q  L  L  K  L  W  K  H  Q  N  K  D  Q  D  I  V  K  K
      910              930              950
GATCATCCAAGATATTGACCTCTGTGAAAACAGCGTGCAGCGGCACATTGGACATGCTAA
  I  I  Q  D  I  D  L  C  E  N  S  V  Q  R  H  I  G  H  A  N
      970              990              1010
CCTCACCTTCGAGCAGCTTCGTAGCTTGATGGAAAGCTTACCGGGAAAGAAAGTGGGAGC
  L  T  F  E  Q  L  R  S  L  M  E  S  L  P  G  K  K  V  G  A
      1030              1050              1070
AGAAGACATTGAAAAACAATAAAGGCATGCAAACCCAGTGACCAGATCCTGAAGCTGCT
  E  D  I  E  K  T  I  K  A  C  K  P  S  D  Q  I  L  K  L  L
      1090              1110              1130
CAGTTTGTGGCGAATAAAAAATGGCGACCAAGACACCTTGAAGGGCCTAATGCACGCACT
  S  L  W  R  I  K  N  G  D  Q  D  T  L  K  G  L  M  H  A  L
      1150              1170              1190
AAAGCACTCAAAGACGTACCACTTTCCCAAACTGTCACTCAGAGTCTAAAGAAGACCAT
  K  H  S  K  T  Y  H  F  P  K  T  V  T  Q  S  L  K  K  T  I
      1210              1230              1250
CAGGTTCTTCACAGCTTCACAATGTACAAATTGTATCAGAAGTTATTTTAGAAATGAT
  R  F  L  H  S  F  T  M  Y  K  L  Y  Q  K  L  F  L  E  M  I
      1270              1290              1310
AGGTAACCAGGTCCAATCAGTAAAAATAAGCTGCTTATAACTGGAAATGGCCATTGAGCT
  G  N  Q  V  Q  S  V  K  I  S  C  L
      1330              1350
GTTTCCTCACAATTGGCGAGATCCCATGGATGATAA
```

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 9E

osteo.frg	M N K W L C C A L L V L L D I I E W T T Q E T L P P K Y L H Y D P E T G H Q L L C D K K C A P G T Y L	50
osteo.frg	M N K W L C C A L L V L L D I I E W T T Q E T L P P K Y L H Y D P E T G R Q L L C D K K C A P G T Y L	50
osteo.frg	M N K W L C C A L L V L L D I S I K W T T Q E T L P P K Y L H Y D E T S H Q L L C D K K C P P G T Y L	50
osteo.frg	K Q H C T V R R K T L C V P C P D H S Y T D S W H T S D E C V Y C S P V C K E L Q S V K Q E C N R T	100
osteo.frg	K Q H C T V R R K T L C V P C P D Y S Y T D S W H T S D E C V Y C S P V C K E L Q T V K Q E C N R T	100
osteo.frg	K Q H C T A K W K T V C A P C P D H Y Y T D S W H T S D E C L Y C S P V C K E L Q Y V K Q E C N R T	100
osteo.frg	H N R V C E C E E G R Y L E I E F C L K H R S C P P G S G V V Q A G T P E R N T V C K K C P D G F F	150
osteo.frg	H N R V C E C E E G R Y L E L E F C L K H R S C P P G L G V L Q A G T P E R N T V C K R C P D G F F	150
osteo.frg	H N R V C E C K E G R Y L E I E F C L K H R S C P P G F V V Q A G T P E R N T V C K R C P D G F F	150
osteo.frg	S G E T S S K A P C I K H T N C S T F G L L L I Q K G N A T H D N V C S G N R E A T Q K C G I D V T	200
osteo.frg	S G E T S S K A P C R K H T N C S S L G L L L I Q K G N A T H D N V C S G N R E A T Q N C G I D V T	200
osteo.frg	S N E T S S K A P C R K H T N C S V F G L L L T Q K G N A T H D N I C S G N S E S T Q K C G I D V T	200

FIG.9F

osteo.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R R R H S S Q E Q T	250
osteo.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R R R H S S Q E Q T	250
osteo.frg	L C E E A F F R F A V P T K I I P N W L S V L V D S L P G T K V N A E S V E R I K R R R H S S Q E Q T	250
osteo.frg	F Q L L K L W K K H Q N R D Q E M V K K I I Q D I D L C E S S V Q R H L G H S N L T T E Q L L A L M E	300
osteo.frg	F Q L L K L W K K H Q N R D Q E M V K K I I Q D I D L C E S S V Q R H L G H S N L T T E Q L L A L M E	300
osteo.frg	F Q L L K L W K K H Q N R D Q E M V K K I I Q D I D L C E S S V Q R H L G H S N L T T E Q L L A L M E	300
osteo.frg	S L P G K K I S P E E I E R T R K T C K S S E Q L L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteo.frg	S L P G K K I S P D E I E R T R K T C K P S E Q L L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteo.frg	S L P G K K V G A E D I E K T I K A C K P S D Q I L K L L S L W R I K N G D Q D T L K G L M Y A L K	350
osteo.frg	H L K T S H F P K T V T H S L R K T M R F L H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteo.frg	H L K A Y H F P K T V T H S L R K T I R F L H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteo.frg	H S K T Y H F P K T V T Q S L K K T I R F L H S F T M Y R L Y Q K L F L E M I G N Q V Q S V K I S C	400
osteo.frg	L	401
osteo.frg	L	401
osteo.frg	L	401

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 10

1tnrr	C	P	Q	-	G	K	Y	I	H	P	Q	N	N	S	I	C	C	T	K	C	H	K	C	G	T	Y	L	Y	N	D	C	P	G	P	G	Q	D	T	D	C	R	E	C	E	S	G	S	F	T	A	S	49
noste	P	P	K	Y	L	H	Y	D	E	E	T	S	H	Q	L	L	C	D	K	C	P	P	C	G	T	Y	L	K	Q	H	C	T	A	K	-	W	K	T	V	C	A	P	C	P	D	H	Y	Y	T	D	S	49
1tnrr	E	N	H	L	R	H	C	L	S	C	S	-	K	C	R	K	E	M	G	Q	V	E	I	S	S	C	T	V	D	R	D	T	V	C	G	C	R	K	N	Q	Y	R	H	Y	W	S	E	N	L	F	98	
noste	W	H	T	S	D	E	C	L	Y	C	S	P	V	C	-	K	E	L	Q	Y	V	K	-	Q	E	C	C	N	R	T	H	N	R	V	C	E	C	K	E	G	R	Y	L	E	I	-	-	E	-	F	93	
1tnrr	Q	C	F	N	C	S	L	C	L	N	G	-	T	V	H	L	S	C	Q	E	K	Q	N	T	V	C	T	-	C	H	A	G	F	F	L	R	E	-	-	-	N	E	C	V	S	C	139					
noste	-	C	L	K	H	R	S	C	P	P	G	F	G	V	V	Q	A	G	T	P	E	R	N	T	V	C	K	R	C	P	D	G	F	F	S	N	E	T	S	S	K	A	P	C	R	K	H	139				

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. II

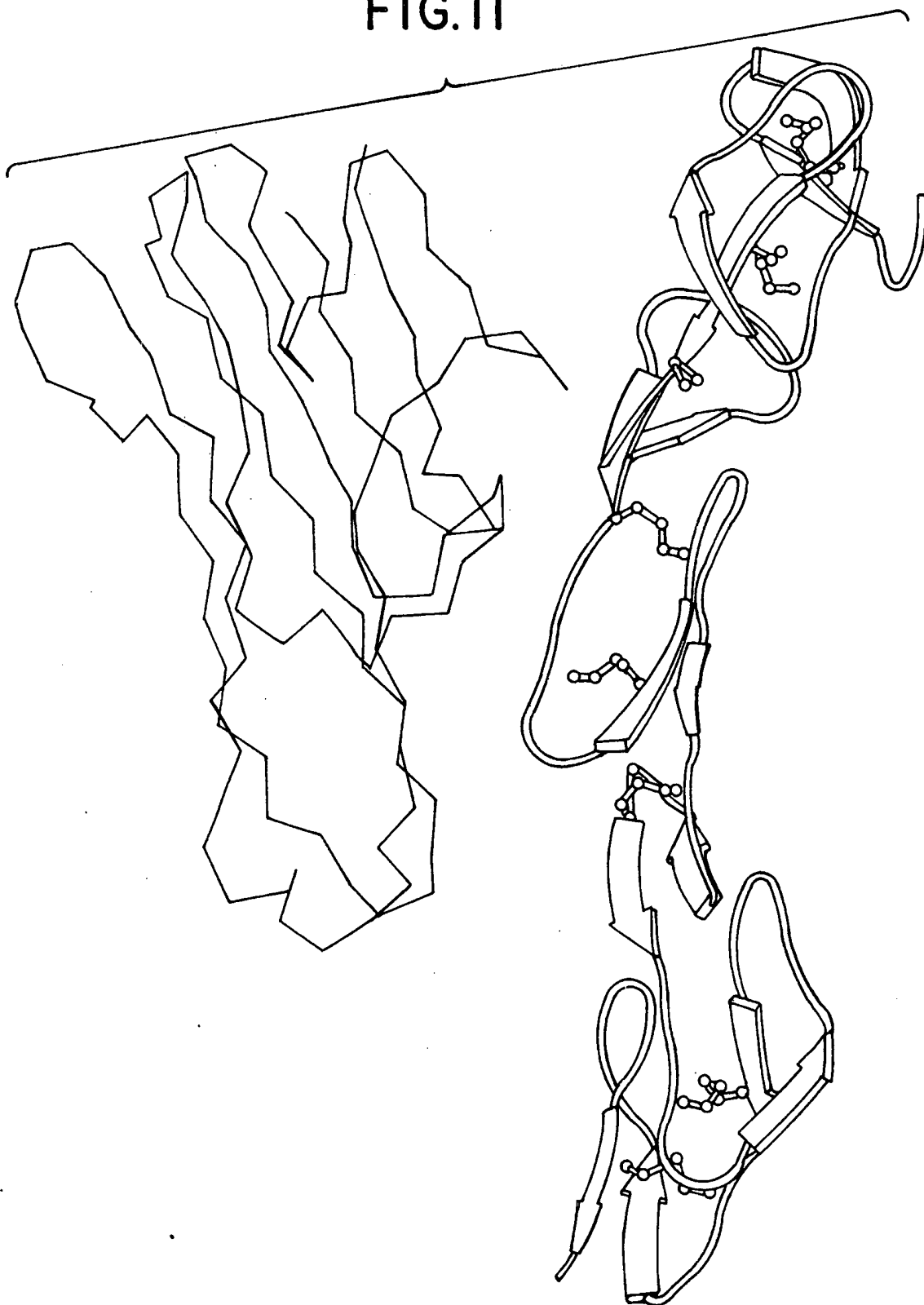
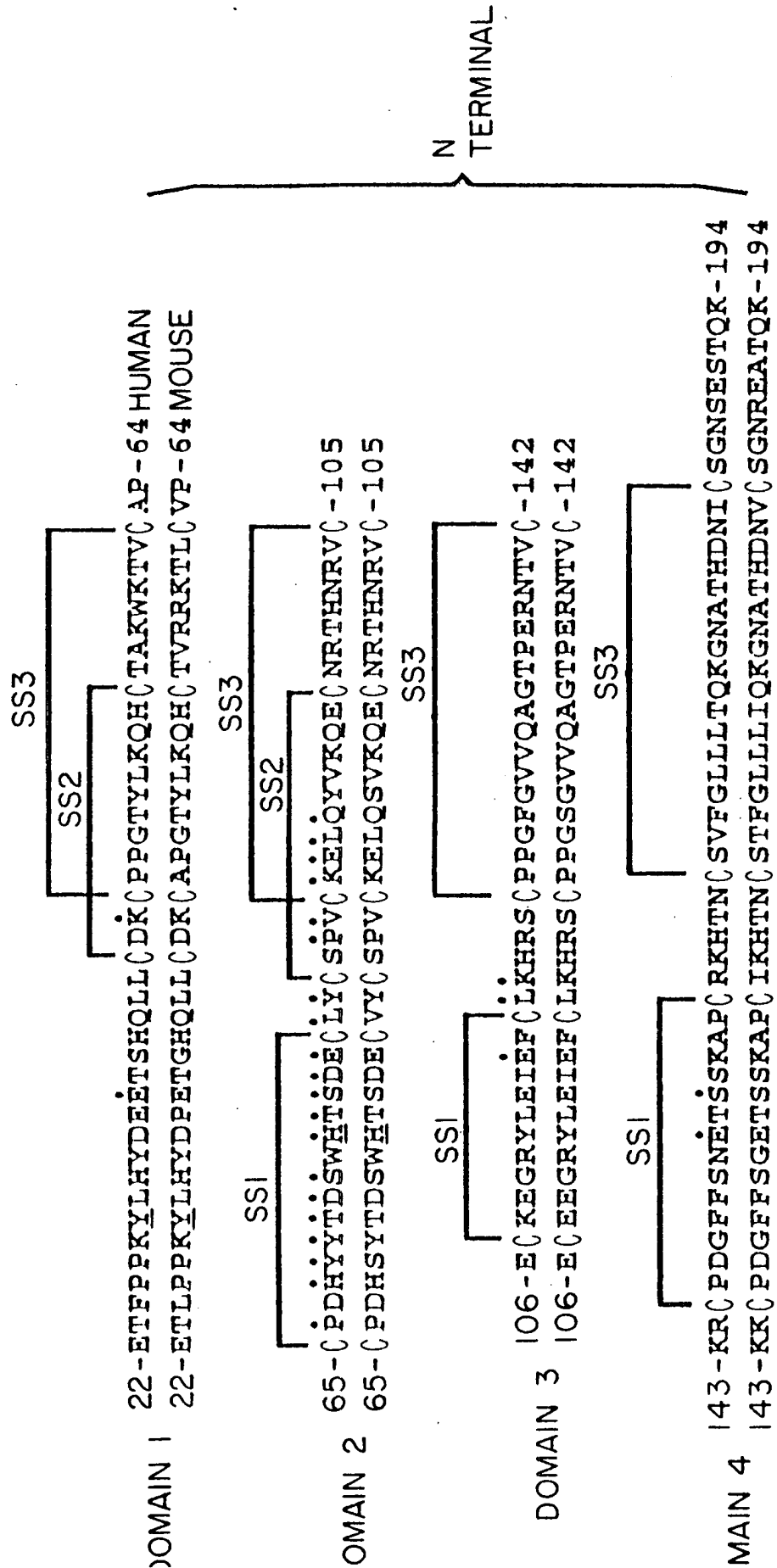


FIG. 12A



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 12B

195-CGIDVTLC^CEEAFFRFAVPTKFTPNWLSVLVDNLPGTKVNAESVERIKRQHSS-246
195-CGIDVTLC^CEEAFFRFAVPTKIIIPNWLSVLVDNLPGTKVNAESVERIKRRHSS-246
247-QEQTFFQLLKLWKHQNKDQDI^CVKKIIQDIDID^CENSVQRHIGHANLTPEQLRSL-298
247-QEQTFFQLLKLWKHQNRDQEMVKKIIQDIDID^CCESSVQRHLGHSNLTTEQLLAL-298
299-MESLPGKKVGAEDIEKTIKAC^CKPSDQILKLLSLWRIKNGDQD^CTLKGLMHALK-350
299-MESLPGKKISPEEIERTRKT^CKSSEQLLKL^CSLWRIKNGDQD^CTLKGLMYALK-350
351-HSKTYHFPKTVTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKIS^CL-401
351-HLKTSHPKTVTHSLRK^CTMRF^CLHSFTMYRLYQKLFLEMIGNQVQSVKIS^CL-401

C
TERMINAL

FIG. 13A



FIG. 13B

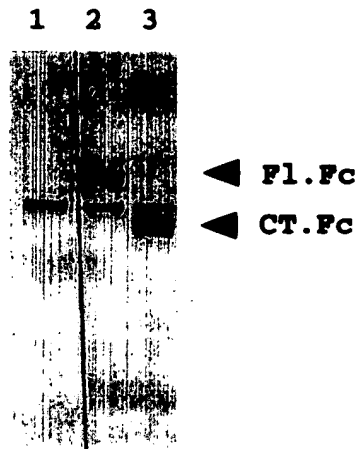


FIG. 13C

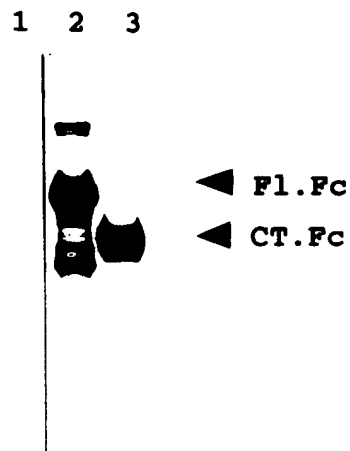


FIG.14A

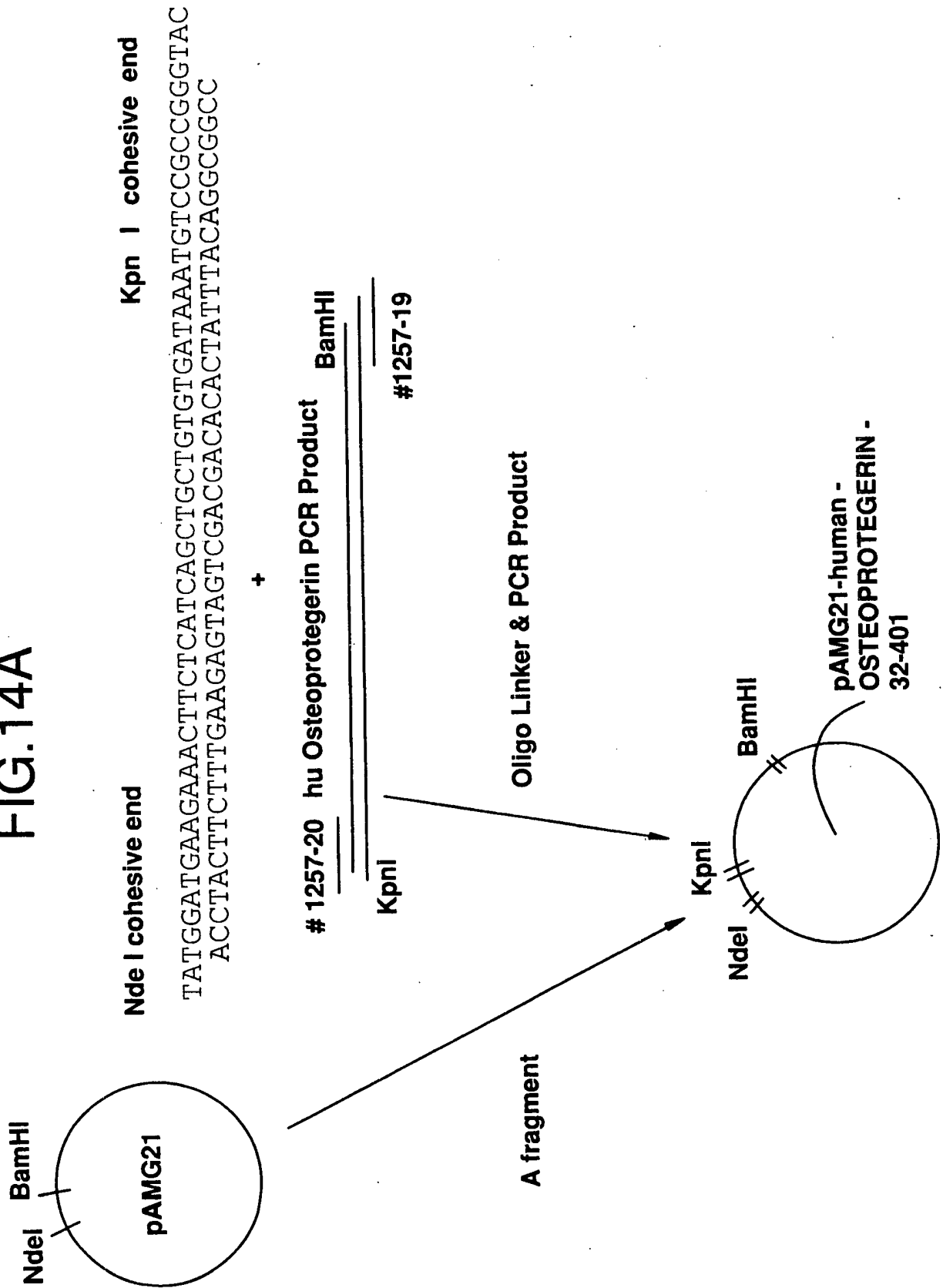
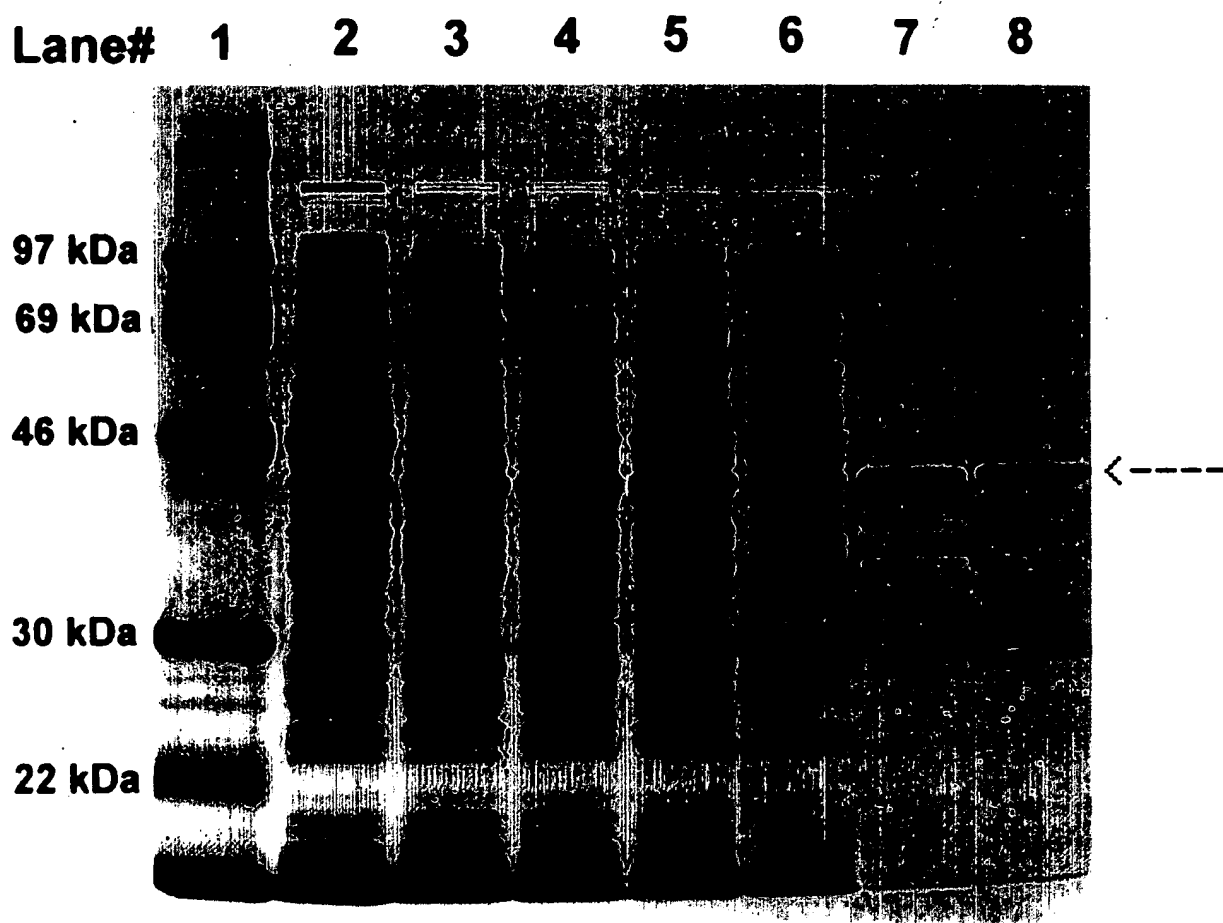
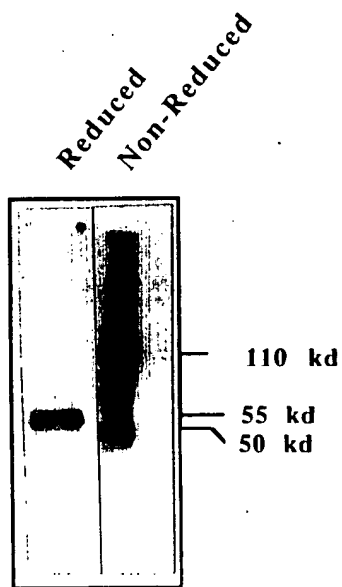


FIG. 14B



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.15



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.16A

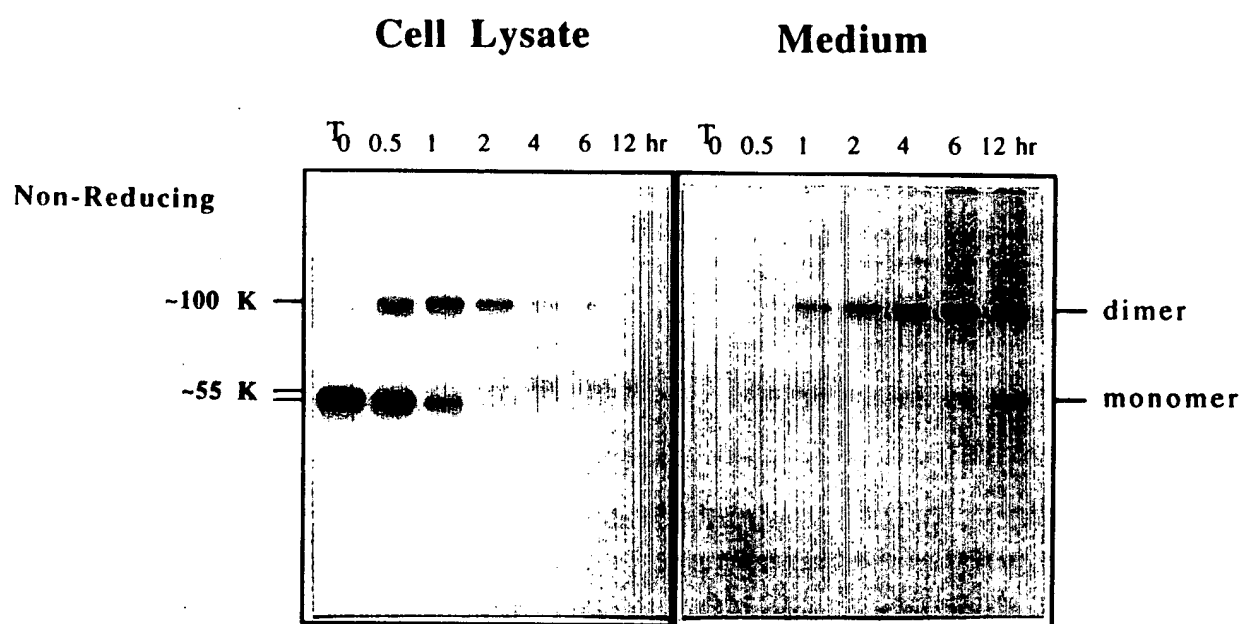
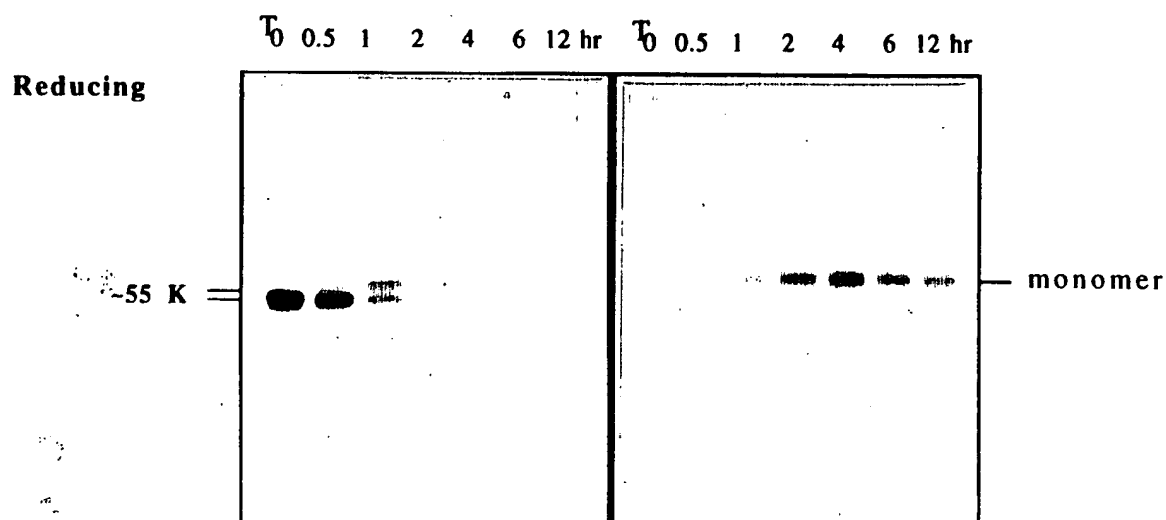


FIG.16B



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.17

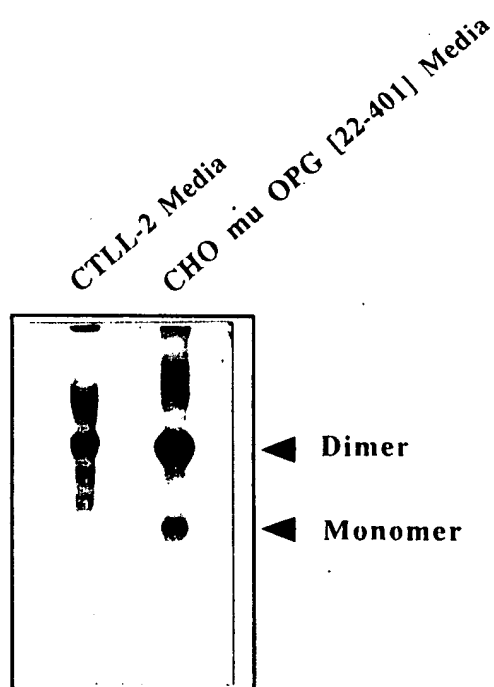


FIG. 18

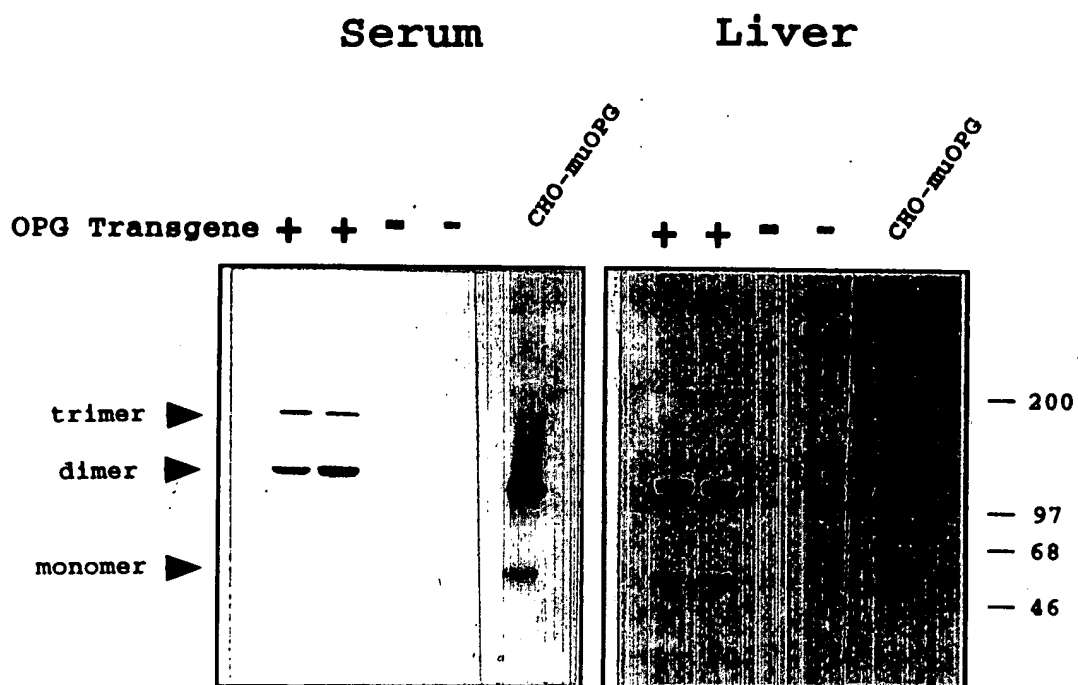


FIG.19A

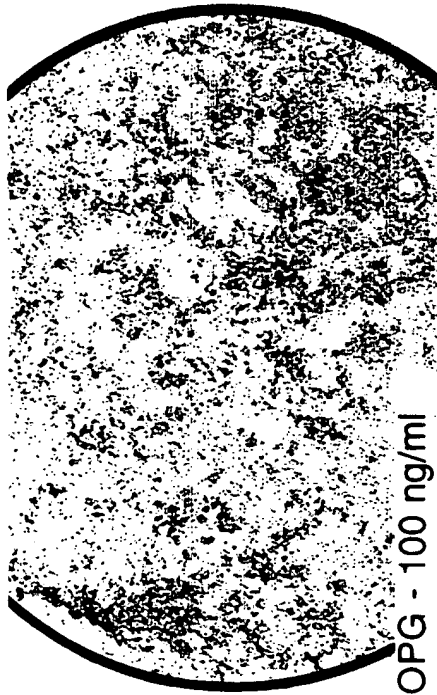


FIG.19B

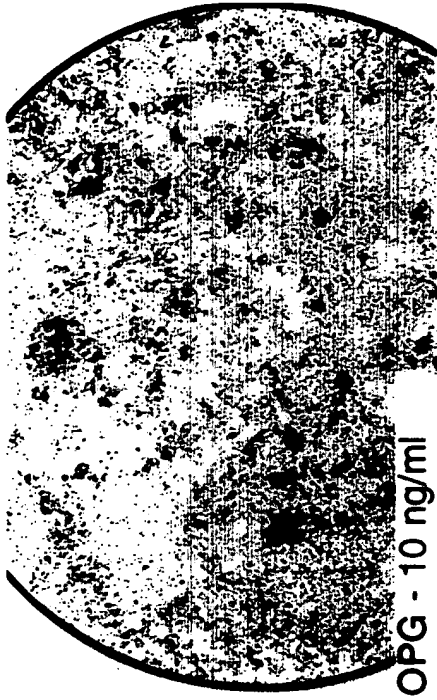


FIG.19C



FIG.19D

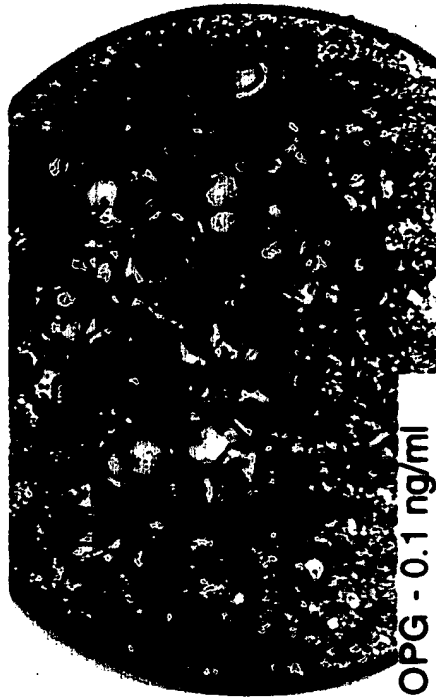


FIG. 19F

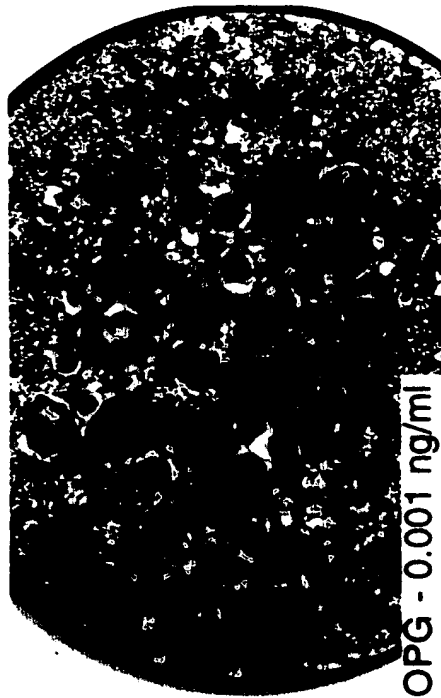


FIG. 19E

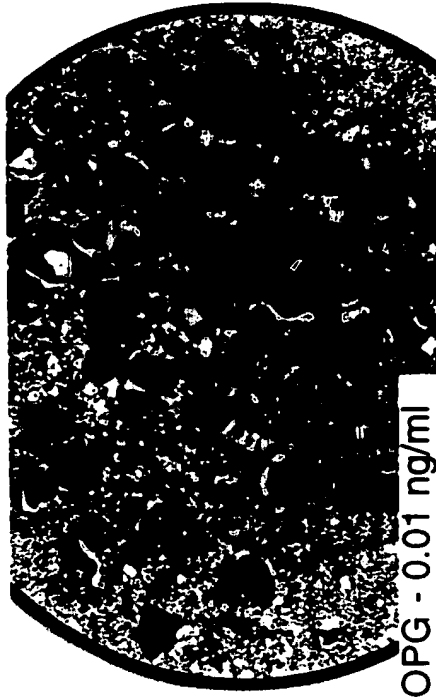


FIG. 19G



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.20

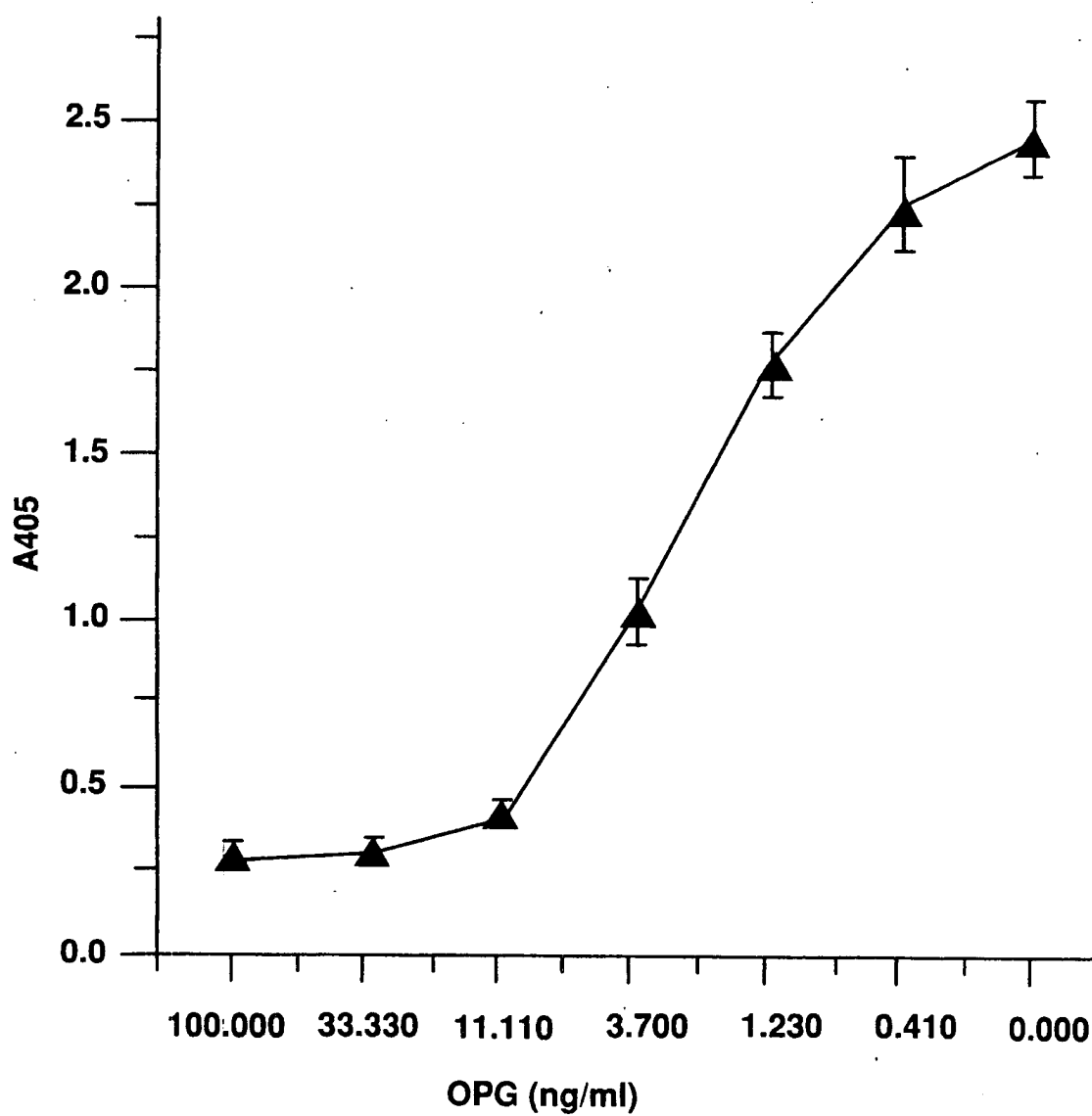
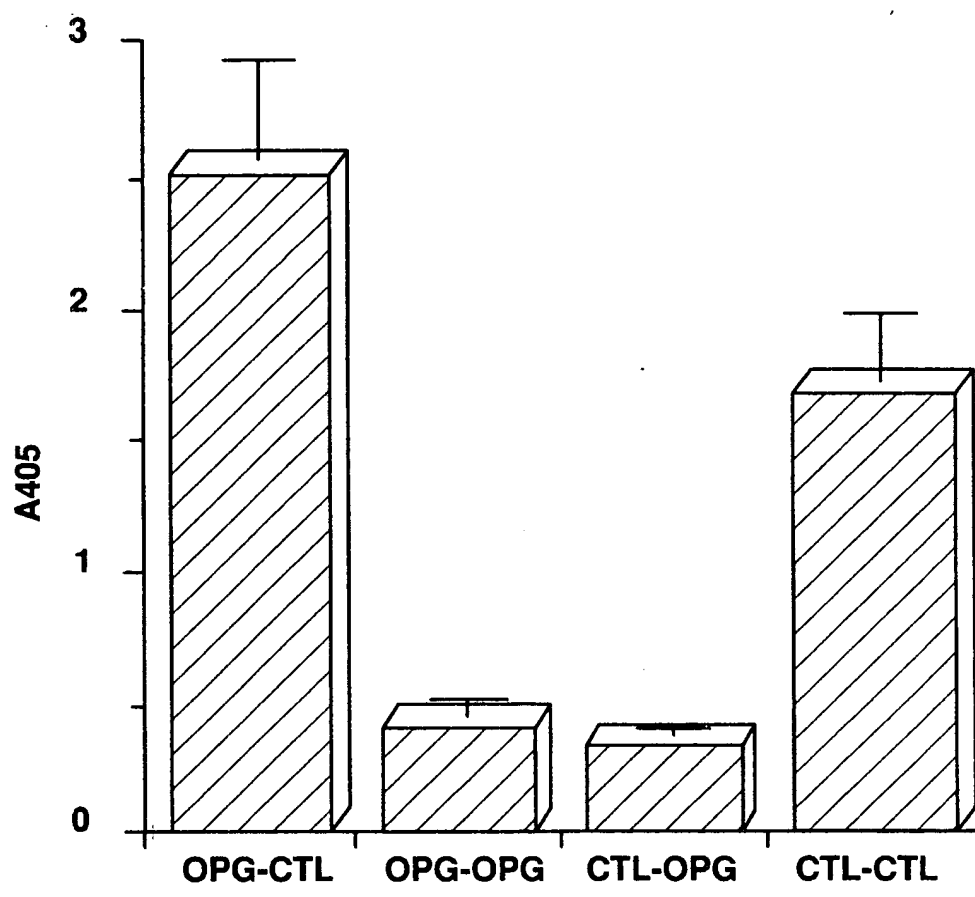


FIG.21



Legend

Growth
Bone marrow
cells
CSF -1

Intermediate
PGE2 + CSF-1

Terminal
ST2 cells
1,25 (OH)2 D3
Dexamethasone

4 days

2 days

8 - 10 days

Groups

CTL - CTL

OPG - CTL

OPG - OPG

OPG - OPG

OPG

100 ng/ml

100 ng/ml

OPG

100 ng/ml

100 ng/ml

FIG.22A

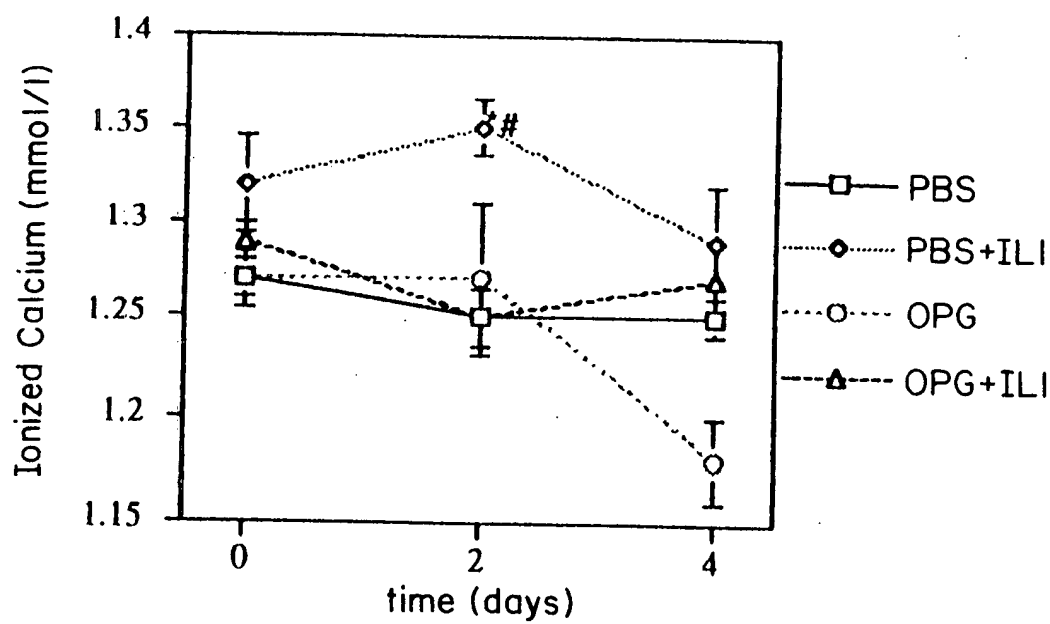
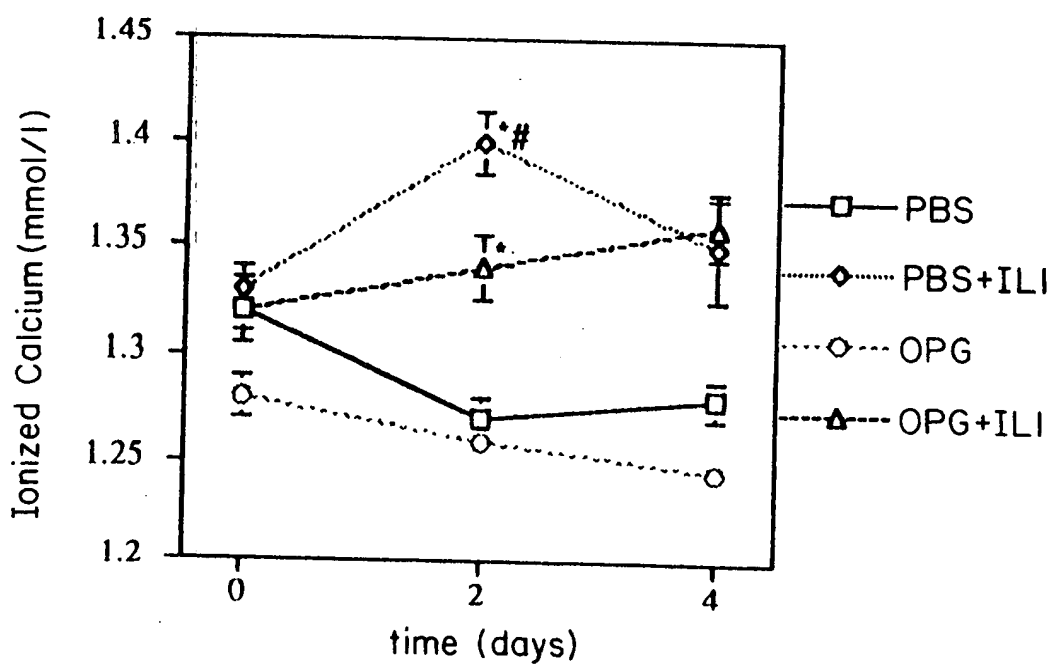


FIG.22B



* Different to PBS, $p < 0.05$

Different to OPG + ILI, $p < 0.05$

FIG.23A

PBS/PBS

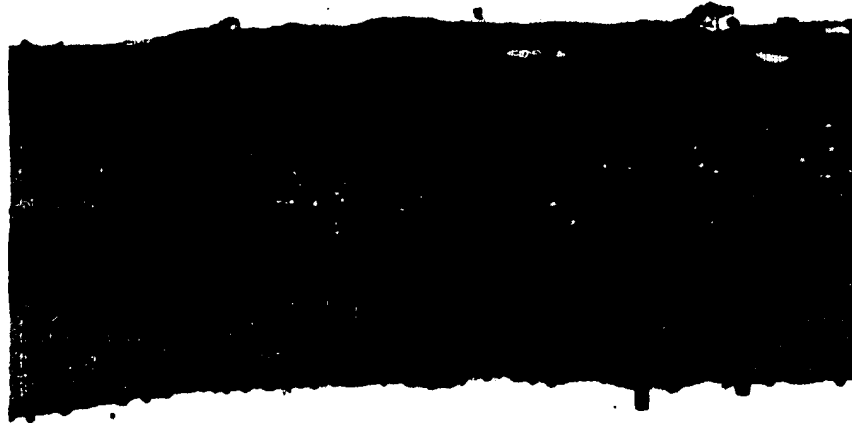


FIG.23B

IL1/PBS

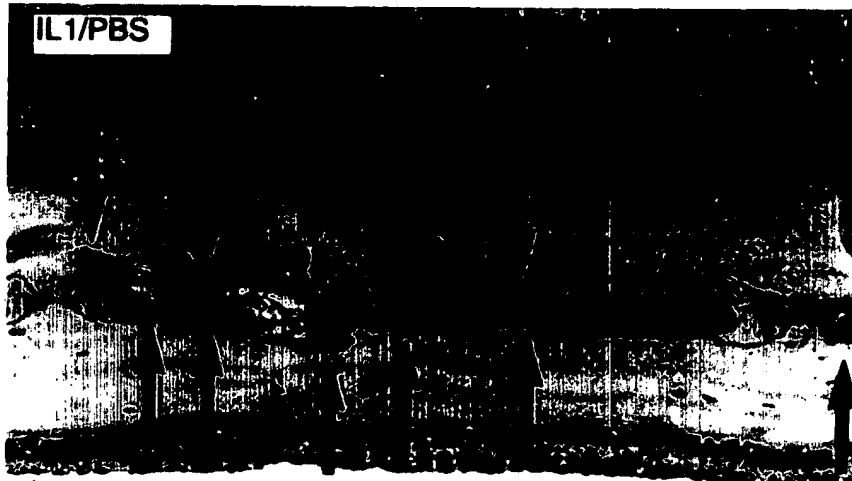


FIG.23C

PBS/OPG

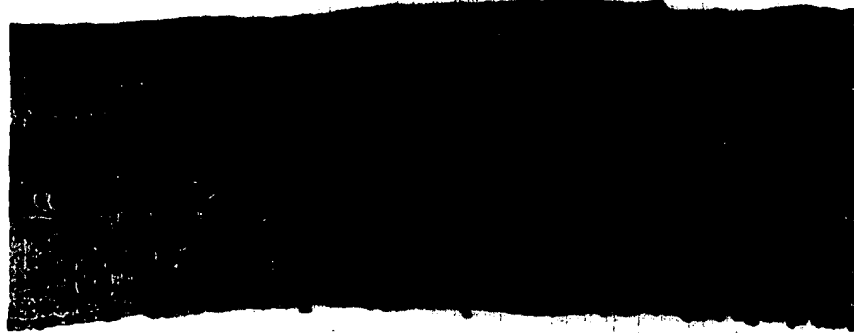


FIG.23D



FIG. 24B

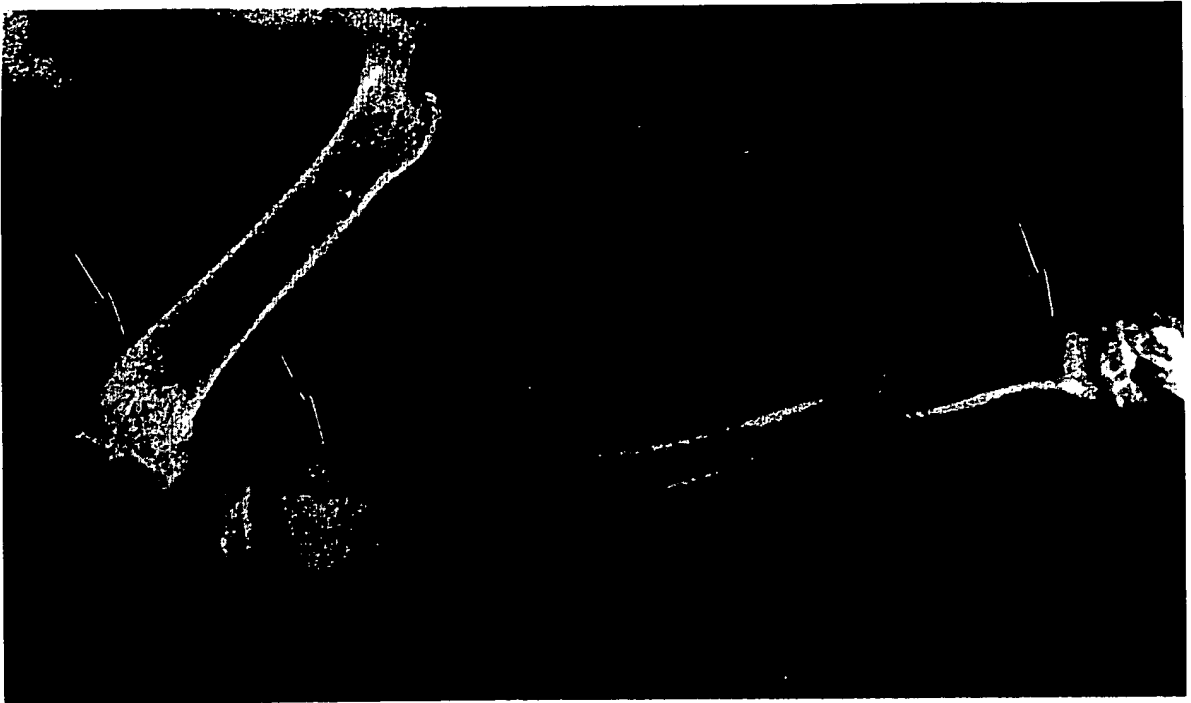
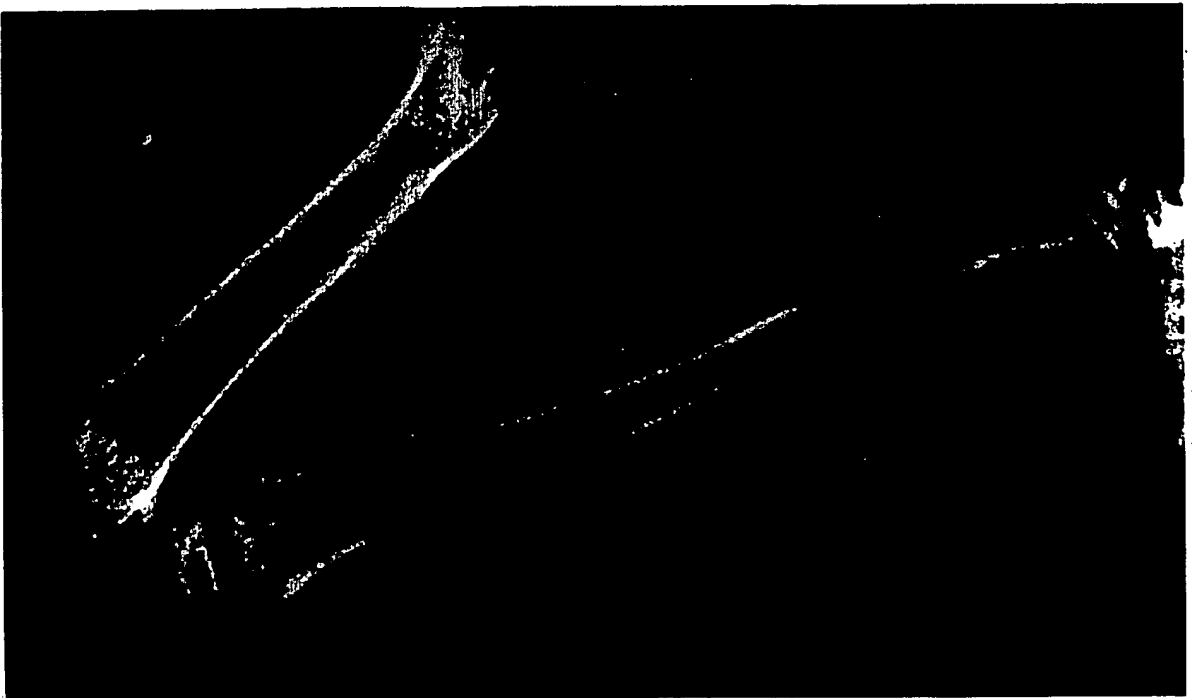
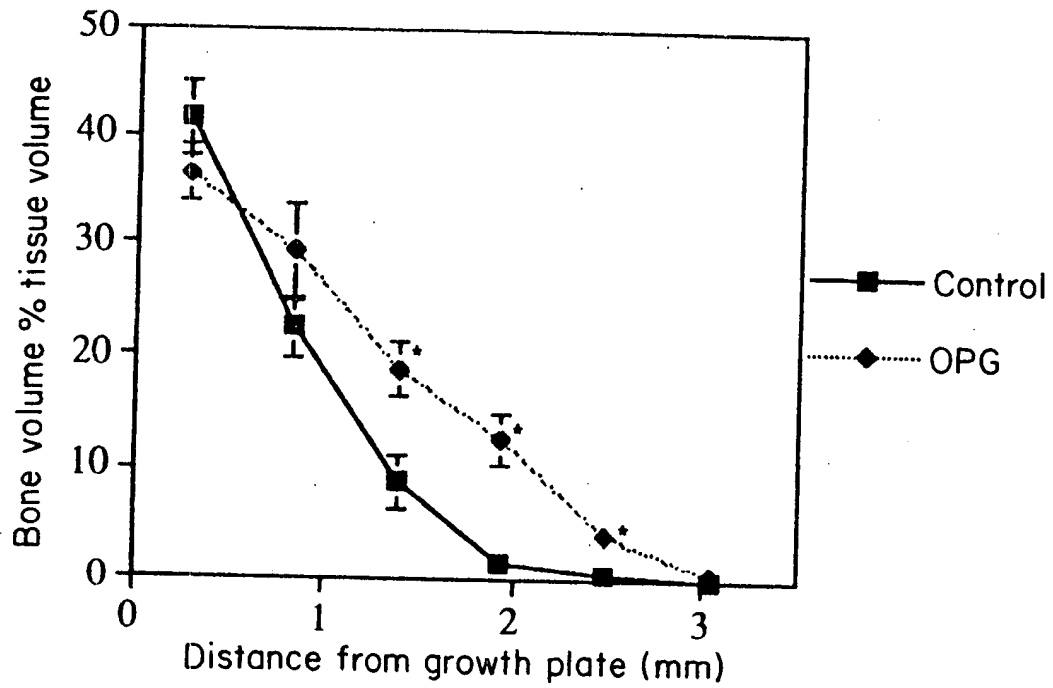


FIG. 24A



TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG.25



* Different to control $p < 0.01$

FIG. 26A



FIG. 26B



FIG.27

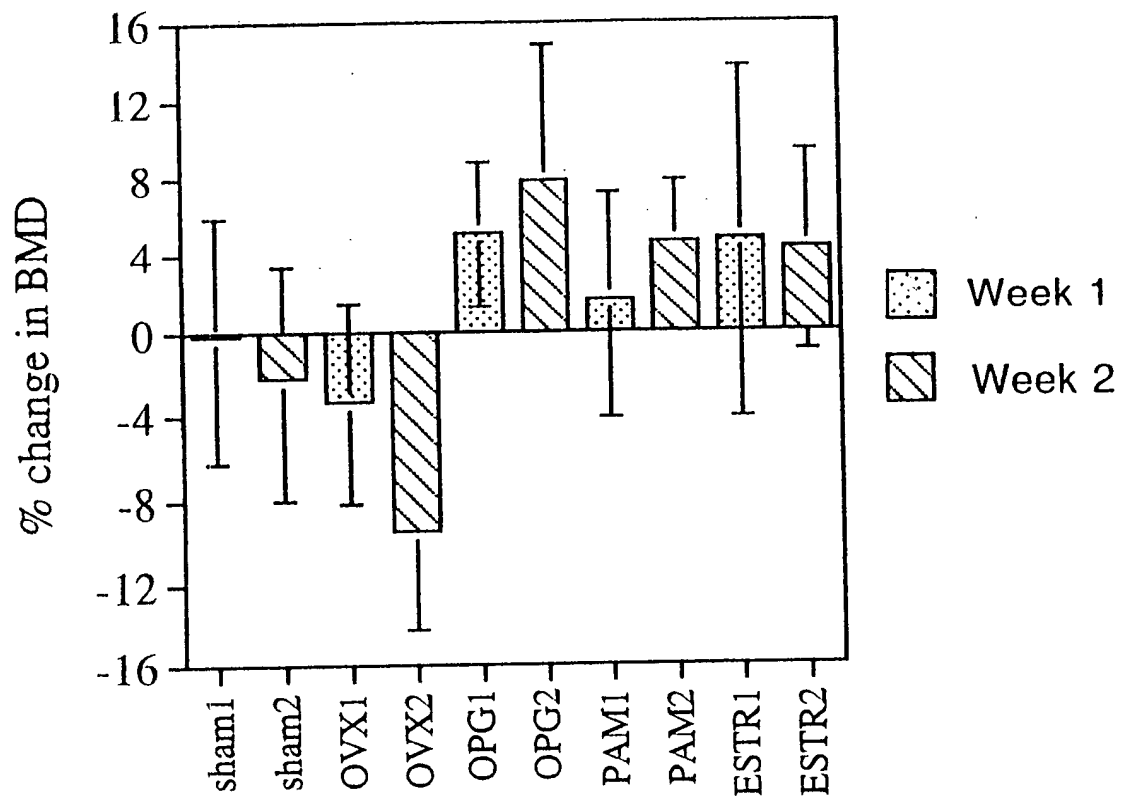
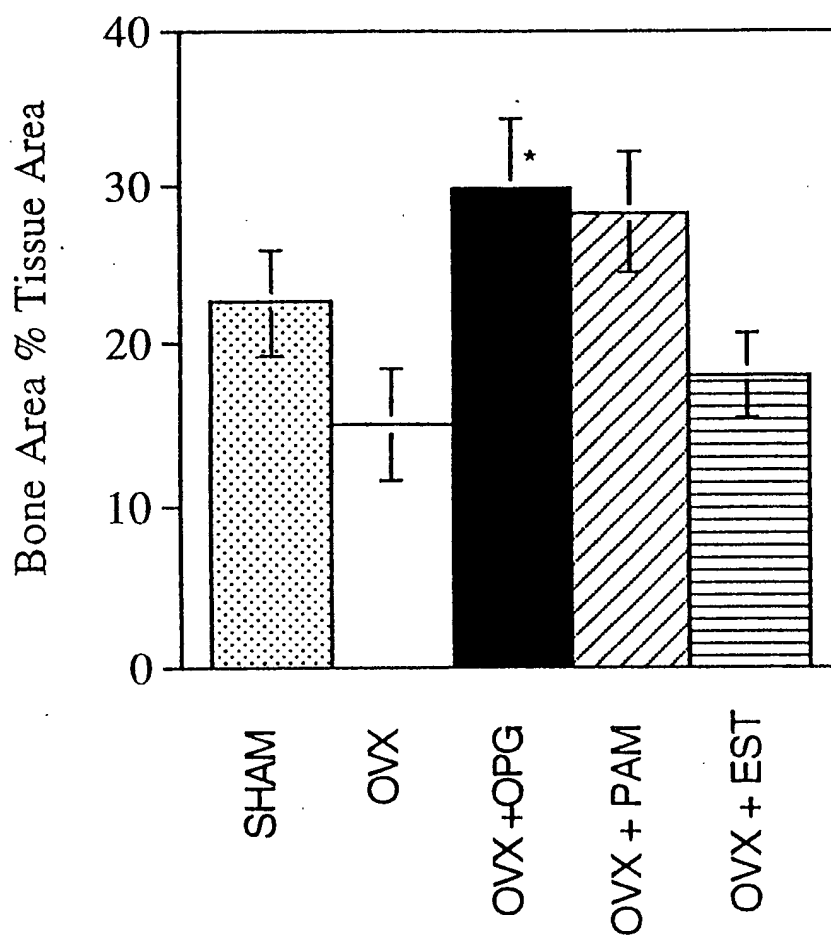


FIG.28



* Different to OVX $p < 0.05$

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29A

DraIII

CATGGGAAATGTCAGAGTGGAGAACCACACCGAGTGCCACTGCAGCACTTGTTATTATCA
1 -----+-----+-----+-----+-----+-----+ 60
GTACCCCTTACAGTCTCACCTCTTGGTGTGGCTCACGGTGACGTCGTGAACAATAATAGT

CAAATCCTAATAGTTTGCAGTGGGCCTTGCTGATGATGGCTGACTTGCTCAAAGGAAAA
61 -----+-----+-----+-----+-----+-----+ 120
GTTTAGGATTATCAAACGTCACCCGGAACGACTACTACCGACTGAACGAGTTTTCCTTTT

TTAATTTGTCCAGTGTCTATGGCTTGTGAGATAAAACCCTCCTTTTCCTTGCCATACCA
121 -----+-----+-----+-----+-----+-----+ 180
AATTAAACAGGTACAGATACCGAAACACTCTATTTTGGGAGGAAAAGGAACGGTATGGT

TTTTTAACCTGCTTTGAGAATATACTGCAGCTTTATTGCTTTTCTCCTTATCCTACAATA
181 -----+-----+-----+-----+-----+-----+ 240
AAAAATTGGACGAAACTCTTATATGACGTCGAAATAACGAAAAGAGGAATAGGATGTTAT

TAATCAGTAGTCTTGATCTTTTCATTGGAATGAAATATGGCATTTAGCATGACCATAAA
241 -----+-----+-----+-----+-----+-----+ 300
ATTAGTCATCAGAACTAGAAAAGTAAACCTTACTTTATACCGTAAATCGTACTGGTATTT

AAGCTGATTCCACTGGAAATAAAGTCTTTTAAATCATCACTCTATCACTGAATTCTAATT
301 -----+-----+-----+-----+-----+-----+ 360
TTCGACTAAGGTGACCTTTATTTTCAGAAAATTTAGTAGTGAGATAGTGAAGTAA

TTTTCTGAAAAGTTTCAAGCCAGTTACTTTTGATAGGATTAACGGAAGGGAGTGAGCCAG
361 -----+-----+-----+-----+-----+-----+ 420
AAAAGACTTTTCAAAGTTCGGTCAATGAAAACATCCTAATTGCCTTCCTCACTCGGTC

XcmI

TGGGTGAGGTGGGTTCCTATGTAGTCAATGGCCTAATACTGGAGAATCTTATTCTAACCA
421 -----+-----+-----+-----+-----+-----+ 480
ACCCACTCCACCCAAGGGTACATCAGTTACCGGATTATGACCTCTTAGAATAAGATTGGT

AGCCTTCCAGAGCAAGCTGTGAGCCCCCTCAGACAGTGGGCTACTCATGAGACAGTCCATT
481 -----+-----+-----+-----+-----+-----+ 540
TCGGAAGGTCTCGTTCGACACTCGGGGAGTCTGTCACCCGATGAGTACTCTGTCAGGTAA

GGGGTAAAGGAAGAAAATATAACTTCTATTTCTATTTCATTTGCACATTGTCTTTAGATGC
541 -----+-----+-----+-----+-----+-----+ 600
CCCCATTTCTTCTTTTATATTGAAGATAAAGATAAGTAAACGTGTAACAGAAATCTACG

CCATTTGGGTGAGTTTTATAGAAGTACAGCTACATTAATAAATAAGAACTGATAATAGATA
601 -----+-----+-----+-----+-----+-----+ 660
GGTAAACCCACTCAAATATCTTCATGTCGATGTAATTTTTTATCTTGACTATTATCTAT

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29B

AGGCTTTAAAAAACTTCATTCATCACCAGTTTGTCAAGATTCCATTTCAAAGTGAAAAA
661 -----+-----+-----+-----+-----+-----+ 720
TCCGAAATTTTTTTGAAGTAAGTAGTGGTCAAACAGTTCTAAGGTAAAGTTTCACTTTTT
CCAATTTCTAACGGGTGGTAAACACAGCAGATGGCAGGGTGAAAAATTAAAGTGAGTGC
721 -----+-----+-----+-----+-----+-----+ 780
GGTTAAAGATTGCCCAACCATTGTGTGCTGTACCGTCCCCTTTTAATTTCACTCACG
ATGTACCTTTAAAGAAACACTGAAATGCACACACATTACTTAACCTGCTCATTCTTTAT
781 -----+-----+-----+-----+-----+-----+ 840
TACATGGAAATTTCTTTGTGACTTTACGTGTGTGTAATGAATTGGACGAGTAAGTAAATA
TTACATATAGTCTTGGGTGTACAAAATTTAGAAATAAATACATATGGGGGCGGGGCCTTA
841 -----+-----+-----+-----+-----+-----+ 900
AATGTATATCAGAACCCACATGTTTTAAATCTTTATTTATGTATACCCCCGCCCCGGAAT
GCTGCACAAATAGGATGCGCGGCGGGCCTTGGTAGGGGCGGAGCCTTAGCTGCACAAATA
901 -----+-----+-----+-----+-----+-----+ 960
CGACGTGTTTATCCTACGCGCCGCGGGAACCATCCCCGCCTCGGAATCGACGTGTTTAT
GGATGCGCGGCGGGCCTTGGTGGGGGCGGGGCTAAGCTGCGCAAGTGGTACACAGCTCA
961 -----+-----+-----+-----+-----+-----+ 1020
CCTACGCGCCGCGGGAACCAACCCCCGCCCCGATTTCGACGCGTTCACCATGTGTGAGT
GGGCTGCGATTTTCGCGCCAACTTGACGGCAATCCTAGCGTGAAGGCTGGTAGGATTTTA
1021 -----+-----+-----+-----+-----+-----+ 1080
CCCGACGCTAAAGCGCGGTTTGAAGTGCCTTAGGATCGCACTTCCGACCATCCTAAAAT
TCCCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCGTGTCCCAAAATATGG
1081 -----+-----+-----+-----+-----+-----+ 1140
AGGGGCGACGGTAGTACCAAGCTGGTAACTTGACGTAGCAGCGGCACAGGGTTTATACC
GGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCC
1141 -----+-----+-----+-----+-----+-----+ 1200
CCTAACCGTTCTTGCTCTGGATGGGACCGGAGGCGAGTCCTTGCTCAAGTTCATGAAGG
AAAGAATGACCACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGA
1201 -----+-----+-----+-----+-----+-----+ 1260
TTTCTTACTGGTGTGGAGAAGTCACCTTCCATTTGTCTTAGACCACTAATACCCATCCT
AAACCTGGTCTCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTTC
1261 -----+-----+-----+-----+-----+-----+ 1320
TTTGGACCAAGAGGTAAGGACTCTTCTTAGCTGGAAATTTCTGTCTTAATTATATCAAG

SacI

BstXI

TCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGCCAAAAGTTTGATG

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29C

AflII
|
ATGCCTTAAGACTTATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAG
1381 -----+-----+-----+-----+-----+-----+ 1440
TACGGAATTCTGAATAACTTGTGGCCTTAACCGTTCATTTTCATCTGTACCAAACCTATC

TCGGAGGCAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAGACTCTTTG
1441 -----+-----+-----+-----+-----+-----+ 1500
AGCCTCCGTCAAGACAAATGGTCCTTCGGTACTTAGTTGGTCCGGTGGAGTCTGAGAAAC

TGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTGGGGA
1501 -----+-----+-----+-----+-----+-----+ 1560
ACTGTTCCCTAGTACGTCCTTAACTTTCACTGTGCAAAAAGGGTCTTTAACTAAACCCCT

AATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGAGGTCCAGGAGGAAAAAGGCA
1561 -----+-----+-----+-----+-----+-----+ 1620
TTATATTTGAAGAGGGTCTTATGGGTCCGCAGGAGAGACTCCAGGTCCTCCTTTTTCCGT

TCAAGTATAAGTTTGAAGTCTACGAGAAGAAAGACTAACAGGAAGATGCTTTCAAGTTCT
1621 -----+-----+-----+-----+-----+-----+ 1680
AGTTCATATTCAAACCTTCAGATGCTCTTCTTTCTGATTGTCCTTCTACGAAAGTTCAAGA

BglII
|
CTGCTCCCCTCCTAAAGCTATGCATTTTTATAAGACCATGGGACTTTTGCTGGCTTTAGA
1681 -----+-----+-----+-----+-----+-----+ 1740
GACGAGGGGAGGATTTGATACGTAATAATATTCTGGTACCCTGAAAACGACCGAAATCT

TCTGAAACACTGAAATTGTCTGCTTCTCATCTTCAGTGAGATTCCAAAGGATAGTACAGT
1741 -----+-----+-----+-----+-----+-----+ 1800
AGACTTTGTGACTTTAACAGACGAAGAGTAGAAGTCACTCTAAGGTTTCCTATCATGTCA

GACAGAACAAGAATAGGCACTCTCTACAAAAAAGAAAGAAAAAACTAAGTAATAGCAA
1801 -----+-----+-----+-----+-----+-----+ 1860
CTGTCTTGTTCTTATCCGTGAGAGATGTTTTTTTCTTTCTTTTGTATTCAATATCGTT

GCATAATAGCTACTGTTAAGAACTCAGAGATAATGAATTGAGAATGGATACTGCTTGAAA
1861 -----+-----+-----+-----+-----+-----+ 1920
CGTATTATCGATGACAATTCTTGAGTCTCTATTACTTAACTCTTACCTATGACGAACTTT

TGAAAATTTAATAAGTTAGAACTAACTTTATAAAAAATAAAAAAATGAGCATTAAAAAA
1921 -----+-----+-----+-----+-----+-----+ 1980
ACTTTTAAATTATTCAATCTTTGATTGAAATATTTTTATTTTTTACTCGTAATTTTTT

NheI
|
AAAAAAAAAAAAAAAAAAAAACCCCCCCCCCCCCCTGCAGCCAAGCTAGCTTGAATC
1981 -----+-----+-----+-----+-----+-----+ 2040

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29D

BspLU11I

AGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAA
2041 -----+-----+-----+-----+-----+-----+ 2100
TCCCCTATTGCGTCCTTTCTTGTACACTCGTTTTCCGGTCGTTTTCCGGTCCTTGGCATT

AAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAA
2101 -----+-----+-----+-----+-----+-----+ 2160
TTTCCGGCGCAACGACCGCAAAAAGGTATCCGAGGCGGGGGGACTGCTCGTAGTGTTTTT

TCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC
2161 -----+-----+-----+-----+-----+-----+ 2220
AGCTGCGAGTTCAGTCTCCACCGCTTTGGGCTGTCCTGATATTTCTATGGTCCGCAAAGG

CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTC
2221 -----+-----+-----+-----+-----+-----+ 2280
GGGACCTTCGAGGGAGCACGCGAGAGGACAAGGCTGGGACGGCGAATGGCCTATGGACAG

CGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAG
2281 -----+-----+-----+-----+-----+-----+ 2340
GCGGAAAGAGGGAAGCCCTTCGCACCGCGAAAGAGTATCGAGTGCGACATCCATAGAGTC

TTCGGTGTAGGTCGTTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTTACGCCCGA
2341 -----+-----+-----+-----+-----+-----+ 2400
AAGCCACATCCAGCAAGCGAGGTTGACCCGACACACGTGCTTGGGGGGCAAGTCGGGCT

CCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC
2401 -----+-----+-----+-----+-----+-----+ 2460
GGCGACGCGGAATAGGCCATTGATAGCAGAACTCAGGTTGGGCCATTCTGTGCTGAATAG

GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTAC
2461 -----+-----+-----+-----+-----+-----+ 2520
CGGTGACCGTCGTCGGTGACCATTGTCCTAATCGTCTCGCTCCATACATCCGCCACGATG

AGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTG
2521 -----+-----+-----+-----+-----+-----+ 2580
TCTCAAGAACTTCACCACCGGATTGATGCCGATGTGATCTTCCTGTCATAAACCATAGAC

CGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACA
2581 -----+-----+-----+-----+-----+-----+ 2640
GCGAGACGACTTCGGTCAATGGAAGCCTTTTTCTCAACCATCGAGAACTAGGCCGTTTGT

HgiEII

AACCACCGCTGGTAGCGGTGGTTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAA
2641 -----+-----+-----+-----+-----+-----+ 2700
TTGGTGGCGACCATCGCCACCAAAAAACAAACGTTTCGTGCTCTAATGCGCGTCTTTTTT

AGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAA
2701 -----+-----+-----+-----+-----+-----+ 2760

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29E

```
CTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTT
2761 -----+-----+-----+-----+-----+-----+ 2820
GAGTGCAATTCCTAAAACCAGTACTCTAATAGTTTTTTCCTAGAAGTGGATCTAGGAAAA

AAATTAAAAATGAAGTTTTTAAATCAATCTAAAGTATATATGAGTAACTTGGTCTGACAG
2821 -----+-----+-----+-----+-----+-----+ 2880
TTTAATTTTTTACTTCAAATTTAGTTAGATTTTCATATATACTCATTTGAACCAGACTGTC

TTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCAT
2881 -----+-----+-----+-----+-----+-----+ 2940
AATGGTTACGAATTAGTCACTCCGTGGATAGAGTCGCTAGACAGATAAAGCAAGTAGGTA

AGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCC
2941 -----+-----+-----+-----+-----+-----+ 3000
TCAACGGACTGAGGGGCAGCACATCTATTGATGCTATGCCCTCCCGAATGGTAGACCGGG

CAGTGCTGCAATGATACCGCGAGACCCACGCTCACC GGCTCCAGATTTATCAGCAATAAA
3001 -----+-----+-----+-----+-----+-----+ 3060
GTCACGACGTTACTATGGCGCTCTGGGTGCGAGTGGCCGAGGTCTAAATAGTCGTTATTT

CCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCCTCCATCCA
3061 -----+-----+-----+-----+-----+-----+ 3120
GGTCGGTCGGCCTTCCCGGCTCGCGTCTTCACCAGGACGTTGAAATAGGCGGAGGTAGGT

GTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC GCAA
3121 -----+-----+-----+-----+-----+-----+ 3180
CAGATAATTAACAACGGCCCTTCGATCTCATTCATCAAGCGGTCAATTATCAAACGCGTT

CGTTGTTGCCATTGCTGCAGGCATCGTGGTGTACGCTCGTCGTTTGGTATGGCTTCATT
3181 -----+-----+-----+-----+-----+-----+ 3240
GCAACAACGGTAACGACGTCCGTAGCACCACAGTGCGAGCAGCAAACCATAACCGAAGTAA

CAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGC
3241 -----+-----+-----+-----+-----+-----+ 3300
GTCGAGGCCAAGGGTTGCTAGTTCCGCTCAATGTACTAGGGGGTACAACACGTTTTTTTCG

                                EaeI
                                |
          PvuI                GdiII
          |                    |
GGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACT
3301 -----+-----+-----+-----+-----+-----+ 3360
CCAATCGAGGAAGCCAGGAGGCTAGCAACAGTCTTCATTCAACCGGCGTCACAATAGTGA

CATGGTTATGGCAGCACTGCATAATTCTCTTACTGTGTCATGCCATCCGTAAGATGCTTTTC
3361 -----+-----+-----+-----+-----+-----+ 3420
GTACCAATACCGTCGTGACGTATTAAGAGAATGACAGTACGGTAGGCATTCTACGAAAAG

                                BcgI
                                |
TGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTG
```

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29F

```
CTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCT
3481 -----+-----+-----+-----+-----+-----+ 3540
GAGAACGGGCCGCGAGTTGTGCCCTATTATGGCGCGGTGTATCGTCTTGAAATTTTCACGA

CATCATTGAAAACGTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCGCTGTTGAGATC
3541 -----+-----+-----+-----+-----+-----+ 3600
GTAGTAACCTTTTGCAAGAAGCCCCGCTTTTGAGAGTTCCTAGAATGGCGACAACCTCTAG

CAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAG
3601 -----+-----+-----+-----+-----+-----+ 3660
GTCAAGCTACATTGGGTGAGCACGTGGGTGACTAGAAGTCGTAGAAAATGAAAGTGGTC

CGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAGGGAATAAGGGCGAC
3661 -----+-----+-----+-----+-----+-----+ 3720
GCAAAGACCCACTCGTTTTTGTCTTCCGTTTTACGGCGTTTTTCCCTTATTCCTCGCTG

SspI
|
ACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGG
3721 -----+-----+-----+-----+-----+-----+ 3780
TGCCTTTACAACCTTATGAGTATGAGAAGGAAAAAGTTATAATAACTTCGTAAATAGTCCC

TTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGT
3781 -----+-----+-----+-----+-----+-----+ 3840
AATAACAGAGTACTCGCCTATGTATAAACTTACATAAATCTTTTATTTGTTTATCCCCA

TCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGAC
3841 -----+-----+-----+-----+-----+-----+ 3900
AGGCGCGTGTAAGGGGGCTTTTCACGGTGGACTGCAGATTCTTTGGTAATAATAGTACTG

ATTAACCTATAAAAATAGGCGTATCACGAGGCCCTTTTCGTCTTCAAGAATTCCTGTGGA
3901 -----+-----+-----+-----+-----+-----+ 3960
TAATTGGATATTTTTATCCGCATAGTGCTCCGGGAAAGCAGAAGTTCTTAAGGGACACCT

ATGTGTGTCAGTTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAA
3961 -----+-----+-----+-----+-----+-----+ 4020
TACACACAGTCAATCCCACACCTTTCAGGGGTCCGAGGGGTCTCCGTCTTCATACGTTT

GCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCA
4021 -----+-----+-----+-----+-----+-----+ 4080
CGTACGTAGAGTTAATCAGTCGTTGGTCCACACCTTTCAGGGGTCCGAGGGGTCTGTCGGT

GAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCCTAACTCCGC
4081 -----+-----+-----+-----+-----+-----+ 4140
CTTCATACGTTTCGTACGTAGAGTTAATCAGTCGTTGGTATCAGGGCGGGGATTGAGGCG

CCATCCCGCCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTT
4141 -----+-----+-----+-----+-----+-----+ 4200
```

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29G

SfiI
|
TTTTTATTTATGCAGAGGCCGAGGCCGCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAG
4201 -----+-----+-----+-----+-----+-----+ 4260
AAAAATAAATACGTCTCCGGCTCCGGCGGAGCCGGAGACTCGATAAGGTCTTCATCACTC

AvrII
|
GAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTGGTCGAGGCTCGCATCTCTCCTT
4261 -----+-----+-----+-----+-----+-----+ 4320
CTCCGAAAAAACCTCCGGATCCGAAACGTTTTTCGACCAGCTCCGAGCGTAGAGAGGAA

CACGCGCCCGCCGCCCTACCTGAGGCCGCCATCCACGCCGGTTGAGTCGCGTTCTGCCGC
4321 -----+-----+-----+-----+-----+-----+ 4380
GTGCGCGGGCGGCGGGATGGACTCCGGCGGTAGGTGCGGCCAACTCAGCGCAAGACGGCG

CTCCCGCCTGTGGTGCTCCTGAACTGCGTCCGCCGTCTAGGTAAGTTTAAAGCTCAGGT
4381 -----+-----+-----+-----+-----+-----+ 4440
GAGGGCGGACACCACGGAGGACTTGACGCAGGCGGCAGATCCATTCAAATTCGAGTCCA

NgoAIV
|
CGAGACCGGGCCTTTGTCCGGCGCTCCCTTGGAGCCTACCTAGACTCAGCCGGCTCTCCA
4441 -----+-----+-----+-----+-----+-----+ 4500
GCTCTGGCCCCGAAACAGGCCGCGAGGGAACCTCGGATGGATCTGAGTCGGCCGAGAGGT

CGCTTTGCCTGACCCTGCTTGCTCAACTCTACGTCTTTGTTTCGTTTTCTGTTCTGCGCC
4501 -----+-----+-----+-----+-----+-----+ 4560
GCGAAACGGA CTGGGACGAACGAGTTGAGATGCAGAAACAAAGCAAAAGACAAGACGCGG

HpaI
|
GTTACAGATCCGTCGAGGAACTGAAAAACCAGAAAGTTAACTGGTAAGTTTAGTCTTTTT
4561 -----+-----+-----+-----+-----+-----+ 4620
CAATGTCTAGGCAGCTCCTTGACTTTTTTGGTCTTTCAATTGACCATTCAAATCAGAAAAA

Psp5II BamHI
| |
GTCTTTTATTTT CAGGTCCCGGATCCGGTGGTGGTGCAATCAAAGAACTGCTCCTCAGTG
4621 -----+-----+-----+-----+-----+-----+ 4680
CAGAAAATAAAGTCCAGGGCCTAGGCCACCACCACGTTTAGTTTCTTGACGAGGAGTCAC

GATGTTGCCTTTACTTCTAGGCCTGTACGGAAGTGTTACTTCTGCTCTAAAAGCTGCTGC
4681 -----+-----+-----+-----+-----+-----+ 4740
CTACAACGGAATGAAGATCCGGACATGCCTTCACAATGAAGACGAGATTTTCGACGACG

HindIII XbaI
| |
AACAGCTTCTAGACCACCATGAACAAGTTGCTGTGCTGCGCGCTCGTGTTTCTGGACAT
4741 -----+-----+-----+-----+-----+-----+ 4800
TTGTTCTGAAGATCTGGTGGTACTTGTTCACGACACGACGCGGAGCACAAAGACCTGTA

BssHII
|

FIG. 29H

CTCCATTAAAGTGGAGACCCAGGAAACGTTTCTCTCCAAAGTACCTTCATTATGACGAAGA
4801 -----+-----+-----+-----+-----+-----+-----+ 4860
GAGGTAATTCACCTGGTGGGTCCTTTGCAAAGGAGGTTTCATGGAAGTAATACTGCTTCT
b S I K W T T Q E T F P P K Y L H Y D E E -

KpnI
|

AACCTCTCATCAGCTGTTGTGTGACAAATGTCTCCTGGTACCTACCTAAACAACACTG
4861 -----+-----+-----+-----+-----+-----+ 4920
TTGGAGAGTAGTCGACAACACACTGTTTACAGGAGGACCATGGATGGATTTTGTGTGAC
b T S H Q L L C D K C P P G T Y L K Q H C -

TACAGCAAAGTGAAGACCGTGTGCGCCCCTTGCCCTGACCACTACTACACAGACAGCTG
4921 -----+-----+-----+-----+-----+-----+ 4980
ATGTCGTTTCACCTTCTGGCACACGCGGGGAACGGGACTGGTGATGATGTGTCTGTCTGAC
b T A K W K T V C A P C P D H Y Y T D S W -

GCACACCAGTGACGAGTGTCTATACTGCAGCCCCGTGTGCAAGGAGCTGCAGTACGTCAA
4981 -----+-----+-----+-----+-----+-----+ 5040
CGTGTGGTCACTGCTCACAGATATGACGTCGGGGCACACGTTCCCTCGACGTCATGCAGTT
b H T S D E C L Y C S P V C K E L Q Y V K -

RleAI BsmI
| |

GCAGGAGTGCAATCGCACCCACAACCGCGTGTGCGAATGCAAGGAAGGGCGCTACCTTGA
5041 -----+-----+-----+-----+-----+-----+ 5100
CGTCCTCACGTTAGCGTGGGTGTTGGCGCACACGCTTACGTTCCCTCCCGCGATGGAAGT
b Q E C N R T H N R V C E C K E G R Y L E -

GATAGAGTTCTGCTTGAAACATAGGAGCTGCCCTCCTGGATTTGGAGTGGTGCAAGCTGG
5101 -----+-----+-----+-----+-----+-----+ 5160
CTATCTCAAGACGAAGTTTGTATCCTCGACGGGAGGACCTAAACCTCACCACGTTTCGACC
b I E F C L K H R S C P P G F G V V Q A G -

BsmBI
|

AACCCAGAGCGAAATACAGTTTGCAAAGATGTCCAGATGGGTTCTTCTCAAATGAGAC
5161 -----+-----+-----+-----+-----+-----+ 5220
TTGGGGTCTCGCTTTATGTCAAACGTTTCTACAGGTCTACCCAAGAAGAGTTTACTCTG
b T P E R N T V C K R C P D G F F S N E T -

GTCATCTAAAGCACCCCTGTAGAAAACACACAAATTGCAGTGTCTTTGGTCTCCTGCTAAC
5221 -----+-----+-----+-----+-----+-----+ 5280
CAGTAGATTTTCGTGGGACATCTTTTGTGTGTTTAACGTCACAGAAACCAGAGGACGATTG
b S S K A P C R K H T N C S V F G L L L T -

BspEI
|

TCAGAAAGGAAATGCAACACACGACAACATATGTTCCGGAAACAGTGAATCAACTCAAAA
5281 -----+-----+-----+-----+-----+-----+ 5340

[illegible]

TITLE: COMBINATION THERAPY FOR CONDITIONS
LEADING TO BONE LOSS
INVENTORS: Boyle, et al.
APPLN. NO: A-378CIP5

FIG. 29J

AarI

CTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCA
5881 -----+-----+-----+-----+-----+-----+ 5940
GAGGCTGCCGAGGAAGAAGGAGATGTCGTTGAGTGGCACCTGTTCTCGTCCACCGTCGT
b S D G S F F L Y S K L T V D K S R W Q Q -

SapI

GGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAA
5941 -----+-----+-----+-----+-----+-----+ 6000
CCCCTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTT
b G N V F S C S V M H E A L H N H Y T Q K -

GAGCCTCTCCCTGTCTCCGGGTAAATGATAACTCGAC
6001 -----+-----+-----+-----+-----+ 6037
CTCGGAGAGGGACAGAGGCCCATTTACTATTGAGCTG
b S L S L S P G K * *

FIG. 30A-1

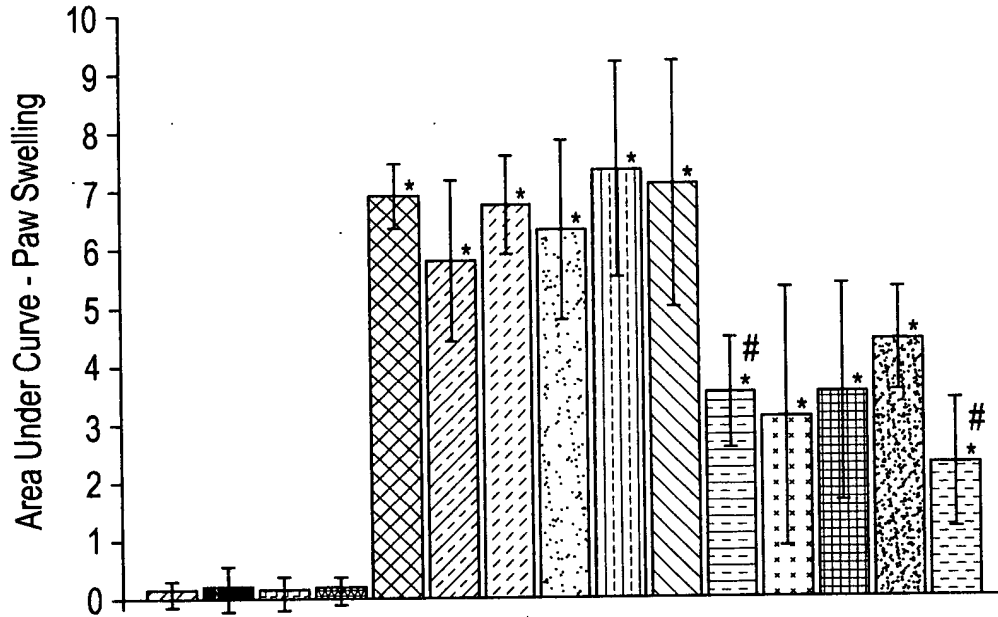
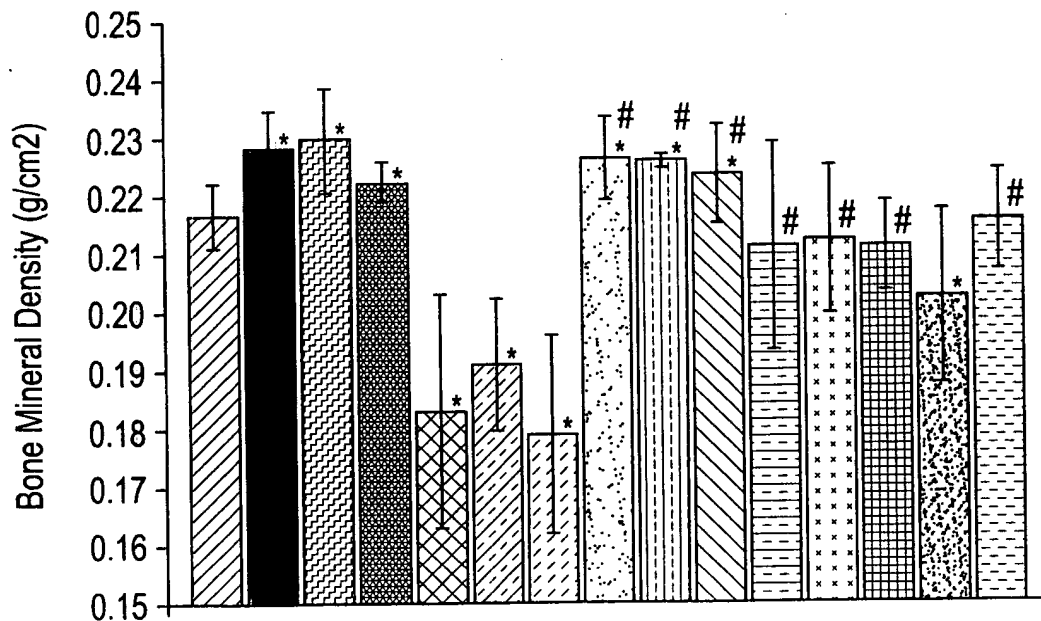


FIG. 30A-2



- | | |
|-----------------------------------|---------------------------------------|
| Normal (NT) | AdA + 1.0 mg/kg OPG-Fc (s.c.) |
| Normal + 4 mg/kg OPG-Fc (s.c.) | AdA + 0.25 mg/kg OPG-Fc (s.c.) |
| Normal + 1.0 mg/kg OPG-Fc (s.c.) | 15.0 mg/kg/hr IL-1ra (2ML1) |
| Normal + 0.25 mg/kg OPG-Fc (s.c.) | 5.0 mg/kg/hr IL-1ra (2ML1) |
| AdA Control | 1.0 mg/kg/hr IL-1ra (2ML1) |
| AdA + CSEP (2ML1) | 0.2 mg/kg/hr IL-1ra (2ML1) |
| AdA + OPG Placebo (s.c.) | AdA + 0.07 mg/kg Dexamethasone (s.c.) |

FIG. 30B-1

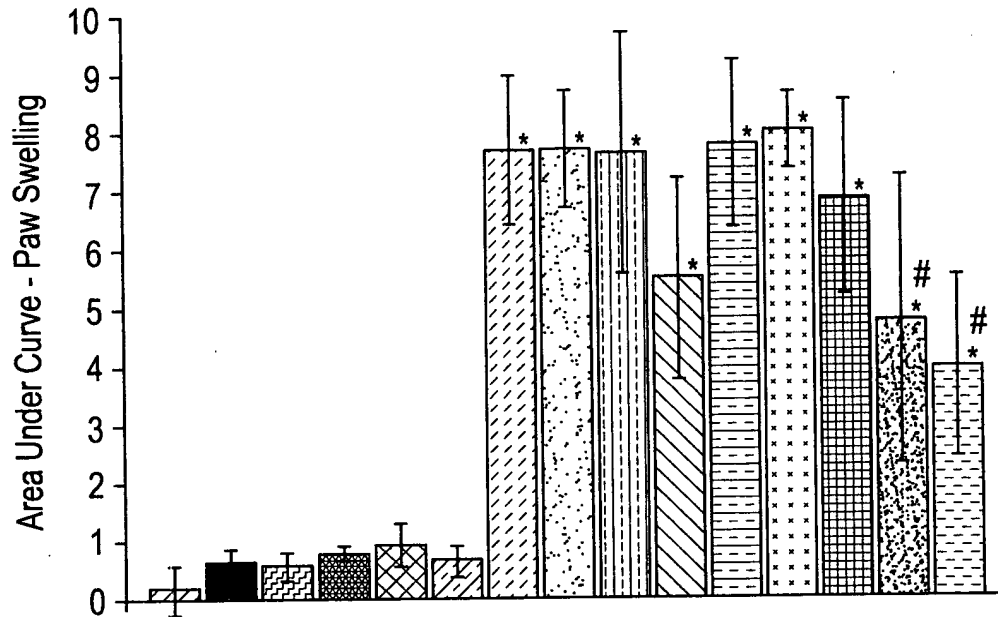
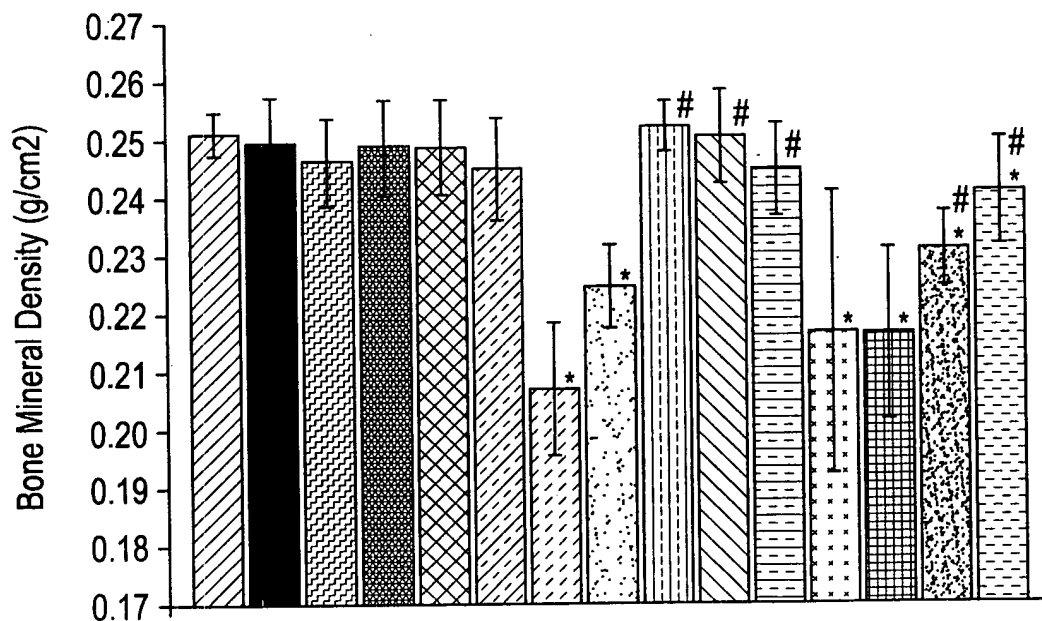


FIG. 30B-2



- | | |
|-------------------------------------|---------------------------------------|
| Normal | AdA + 1.0 mg/kg OPG-Fc (s.c.) |
| Normal + 1.0 mg/kg OPG-Fc (s.c.) | AdA + 0.25 mg/kg OPG-Fc (s.c.) |
| Normal + 0.25 mg/kg OPG-Fc (s.c.) | AdA + 0.0625 mg/kg OPG-Fc (s.c.) |
| Normal + 0.0625 mg/kg OPG-Fc (s.c.) | AdA + 0.016 mg/kg OPG-Fc (s.c.) |
| Normal + 0.016 mg/kg OPG-Fc (s.c.) | AdA + 0.004 mg/kg OPG-Fc (s.c.) |
| Normal + 0.004 mg/kg OPG-Fc (s.c.) | AdA + 5.0 mg/kg/hr IL-1ra (2ML1) |
| AdA control | AdA + 0.07 mg/kg Dexamethasone (s.c.) |

FIG. 31A

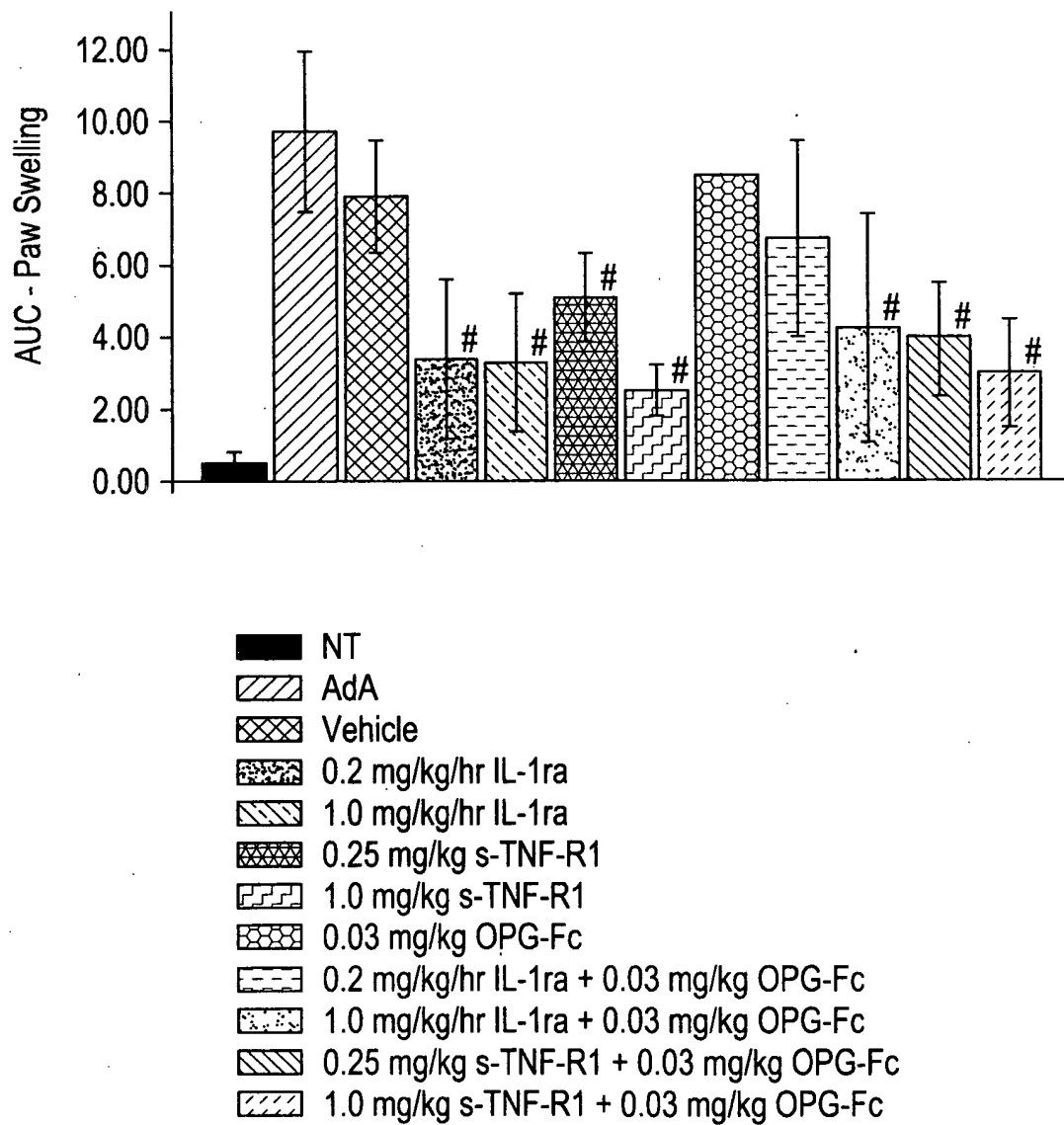


FIG. 31B

